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ERYTHEMA NODOSUM*

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NEW YORK CITY

DURING the years 1928–1941, 88 patients were discharged from the Mount Sinai Hospital, New York City, with a diagnosis of erythema nodosum. These cases were reviewed from two standpoints: to analyze the clinical data from the point of view of associated diseases; and to determine whether any specificity to the mediastinal or hilar adenopathy, or both, is shown roentgenologically.

ETIOLOGY AND INCIDENCE

The etiology of erythema nodosum, a doubtful tuberculide, is not known. Originally, it was believed to be an acute specific febrile and mildly communicable disease. Accumulating evidence (Spink[1] and Paul and Pohle[2]) suggests that it is not a specific pathologic entity but a nonspecific toxic complex with many precipitating or provoking factors. It may occur during the course of various conditions, both infectious and noninfectious.

It is three to five times more prevalent in females and most frequent in young persons. It is rare in children under the age of three and in very old people. It is most prevalent during the spring season. The incidence of erythema nodosum, as well as the type of disease it is associated with, varies with the habitat, type and age of the patients, according to other series reported in the literature.

Wallgren[3] has shown that in Scandinavian children 95 per cent of the cases of erythema nodosum appear with tuberculosis; in England, this percentage is 70, and in this country it is lower. He believes that in tuberculous children the erythema nodosum appears when the child becomes tuberculin sensitive.

In adults, less emphasis has been placed on tuberculosis as an etiologic factor and more on rheumatic fever and streptococcal infections (Paul and Pohle[2]). Keil,[4] after a critical study of the subject, believes that erythema nodosum is not of rheumatic origin.

Dickson[5] has called attention to the association of erythema nodosum and coccidioidomycosis as seen in the San Joaquin Valley, where the latter is known as "valley fever" or "desert fever."

PATHOLOGY

Grossly, the lesions of erythema nodosum consist of discrete, firm, hot, tender conical elevated nodules about 1 to 5 cm. in diameter and symmetrically distributed. The lesions appear most frequently over the anterior aspects of the legs and less frequently over the forearms, arms, thighs, buttocks and face. The average case shows about eight to ten nodules, which have a glossy surface and vary from a bright red to a deep purple. As the nodules begin to regress, they undergo the color involutions of a bruise or contusion.

Histologically, these erythematous nodules suggest nonspecific inflammation. Ormsby[6] describes the changes as "vascular dilatation, marked edema of the collagen, small round-cell infiltration, largely perivascularly arranged in the middle and lower portions of the corium and to a lesser extent in the papillary and subpapillary portions." He also points out that epidermal changes are usually absent.

ANALYSIS OF CASES

This analysis is based on a clinical diagnosis of erythema nodosum made on discharge from the hospital. The patients did not come under our personal clinical observation. In this series of 88 cases, the condition was three times more prevalent in females, and the ages of the patients ranged from two to fifty-eight years (Table 1).

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Associated Diseases

Many diseases and conditions were found to be associated with erythema nodosum. Often, two or more conditions or complaints occurred in the same patient, either preceding or during an attack.

TABLE 1. *Age and Sex Distribution in 88 Cases of Erythema Nodosum.*

AGE	FEMALE NO. OF CASES	MALE NO. OF CASES	TOTAL
yr.			
1–9	7	7	14
10–19	10	7	17
20–29	22	3	25
30–39	10	2	12
40–49	8	0	8
50–59	9	3	12
Totals	66	22	88

In 13 cases, no evidence of associated disease was present. The remaining 75 cases were found to be associated with the following conditions.

Tuberculosis. Four cases were associated with tuberculosis.

The first patient, a five-year-old boy, entered the hospital on November 17, 1928, with two soft-tissue masses, one in the region of the elbow and the other in the region of the ankle. Tubercle bacilli were recovered from the aspirated contents of the soft-tissue masses. Enlargement of the cervical, axillary, epitrochlear, inguinal and submaxillary lymph nodes was found. There was no pulmonary infiltration or mediastinal or hilar adenopathy in the chest roentgenograms. The patient died fourteen months later as the result of tuberculous meningitis.

The second patient, a six-year-old boy (Case 11, Table 2), had enlargement of the mediastinal and hilar nodes on the first roentgenogram of the chest. Eighteen days later, the chest was reexamined and showed, in addition to the previous findings, widespread nodular pulmonary infiltrations bilaterally. The tuberculin test was strongly positive. Autopsy performed at another hospital eight months later showed hematogenous miliary tuberculosis involving the lungs, meninges and practically all the other viscera. The mediastinal and hilar lymph nodes were involved by caseous tuberculosis.

The third patient (Case 7, Table 2), a nine-year-old boy, showed a pneumonic infiltration extending from the left root to the periphery of the left upper lobe and enlarged hilar nodes. The tuberculin test was strongly positive. Physical examination revealed enlargement of the cervical and epitrochlear lymph nodes. The clinical discharge diagnosis was childhood pulmonary tuberculosis. The patient failed to report for follow-up studies.

The fourth patient (Case 14, Table 2), a thirty-four-year-old woman, had been under observation in the Out Patient Department for the previous ten years. A tuberculin test performed seventeen days after the onset of erythema nodosum yielded a strongly positive local reaction, with generalized symptoms of malaise, fever and so forth. Seventeen days later, or thirty-four days after the appearance of the erythematous nodules, one of the lesions on the right leg ulcerated. Biopsy of one of the lesions on this leg showed the changes of erythema nodosum. A roentgenogram of the chest revealed numerous fibrocalcified areas in both upper lobes. Calcifications in the cervical nodes were also seen on the left side of the neck. There was no evidence of recent pulmonary infiltration or consolidation, and guinea-pig inoculation of the gastric contents revealed no evidence of tuberculosis. Within several months, three additional crops of erythematous nodules appeared. The chest roentgenogram remained the same.

Rheumatic heart disease. Of the 7 patients with definite rheumatic heart disease, 2 developed the erythematous lesions while in the hospital during episodes of cardiac decompensation.

There were 10 additional patients with questionable rheumatic heart disease. In 1, in whom rheumatic nodules developed on the ninth and twenty-first days of hospitalization, there was no evidence of heart disease. In the region of the elbows, the nodules of erythema nodosum and the rheumatic nodules were present simultaneously, but were easily differentiated clinically. When this patient returned for follow-up study two years later, there was still no evidence of heart involvement.

Chest roentgenograms were taken in 6 of the 7 cases associated with definite rheumatic heart disease, and in none of these were there any intrathoracic abnormalities, such as enlarged nodes and pulmonary infiltration.

Upper respiratory infection. Most of the 49 cases in this group were associated with upper respiratory infections of streptococcal origin. This group included cases of so-called "grippe," pharyngitis, tonsillitis, sinusitis, peritonsillar abscess and bronchitis. The majority of these patients entered the hospital with a history of illness lasting from a few days to about two weeks. Half showed evidence of peripheral lymphadenopathy. Chest roentgenograms were made in 34 cases of this group, and in 11 there was evidence of enlarged mediastinal or hilar nodes. Clinically, 5 patients of the latter group also had enlargement of the cervical nodes.

Arthralgias. In erythema nodosum, the complaint of joint pain or arthralgia is difficult to evaluate. One must attempt, and often one is unable, to differentiate a true joint pain from pain that is secondary to the inflammatory changes brought about by the erythematous lesions, particularly when the lesions occur in the vicinity of joints. In this series, 28 patients complained of joint pains. There was no abnormality in the 14 patients whose chests were examined by x-ray.

Ulcerative colitis. Six patients with acute or chronic ulcerative colitis developed lesions of erythema nodosum. The chest was examined roentgenologically in only 1 case, in which no abnormality was shown.* Another case of ulcerative colitis, which was not included in this survey, developed lesions that resembled erythema nodosum, but the diagnosis of acute perivasculitis was not excluded.

Drug ingestion. In only 2 patients of a group of 8 with a history of drug ingestion was there strong evidence that the eruption was due to drug intoxication. In both cases, bromides were found in the urine, and in 1 there was a past history of veronal poisoning. The drugs that were found to be related to or ingested prior to the appearance of erythema nodosum were bromides, coal-tar derivatives, potassium iodide, sulfanilamide, Neoprontosil and sulfathiazole. One patient received therapeutic doses of sulfanilamide for three days before the onset of the eruption. This patient was being treated for a prostatic abscess. Another had received 60 gr. of sulfanilamide before the appearance of the erythema nodosum.

In this group of 8 cases, only one roentgenogram of the chest was available, in which no abnormality was noted.

Syphilis. Four patients presented past histories of syphilis, but in none of these was the blood Wassermann or Kahn test positive. Roentgenographically, 1 case (Case 4, Table 2) showed a resolving left-lower-lobe pneumonia, with moderate enlargement of the bronchial nodes bilaterally. Chest roentgenograms of 2 other patients in this group showed no abnormality.

Gonorrhea. None of the 4 patients with past histories of gonorrhea showed evidence of active infection except, perhaps, for the patient with a prostatic abscess, alluded to previously, who received sulfanilamide prior to the occurrence of erythema nodosum.

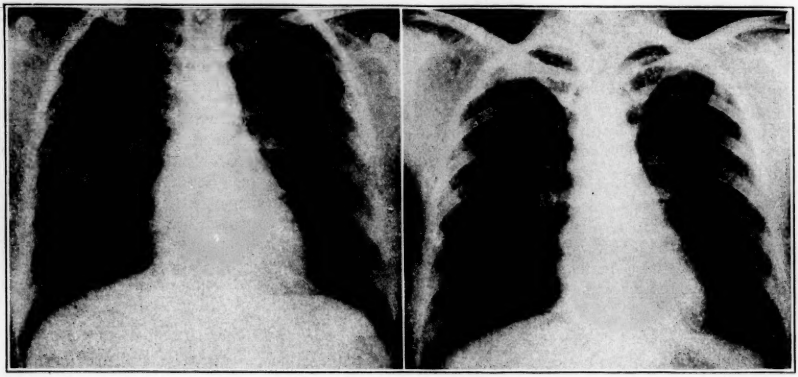

FIGURE 1.

The x-ray film on the left shows enlargement of the mediastinum and hilar lymph nodes in a case of erythema nodosum in which there was no demonstrable associated pulmonary disease; the film on the right was taken four weeks later, when there was essentially no adenopathy.

Herpes zoster. One patient developed herpes zoster on the dorsum of a hand in the same region as the lesions of erythema nodosum twenty-six days after the onset of the erythema. The roentgenogram of the chest was normal.

Measles and otitis media. One patient stated that the onset of erythema nodosum was preceded by measles and bilateral otitis media three weeks and two weeks, respectively, before hospitalization. The chest roentgenogram was normal.

Eye diseases. Conjunctivitis was present in 4 cases. One of these patients had ulcerative colitis a year previously. Another developed an epi-

scleritis during the course of the eruption, and also developed iridocyclitis two months following discharge from the hospital. Of this group of 5 patients, chest films were available in 4 cases, none of which showed any abnormality.

Prostatic abscess. This patient, previously referred to in the section dealing with drug ingestion, stated that he had had gonorrhea thirty years before entering the hospital in 1940 with a prostatic abscess. Roentgenologic examination of the chest was not performed on this patient.

Postoperative infection. Erythema nodosum lesions were described in a patient who had developed a wound infection following a surgical procedure for repair of an incisional hernia.

Axillary abscess. One patient, a nurse, developed erythema nodosum during the course of an axillary abscess. An axillary lymph node was removed histologically, and the findings are described below. The chest of this patient was not examined roentgenologically.

Peritonsillar abscess. While being treated for a peritonsillar abscess, one patient developed the lesions of erythema nodosum. Roentgenologic examination of the chest showed no abnormality.

Tuberculin Tests

Of the forty-four tuberculin tests* that were performed on half the patients, thirty-three were positive. No tests were performed subsequent to discharge from the hospital.

Previous Attacks

Five patients entered the hospital with histories of previous episodes of erythema nodosum. Three patients stated that they had had two, four and five previous attacks respectively, whereas 2 claimed that they had had one previous attack each. Another case had a questionable previous attack.

Subsequent Attacks

Two patients of the group returned with attacks of erythema nodosum. The patient with evidence of bilateral fibrocalcific tuberculosis developed three subsequent crops of erythematous lesions within a period of about five months following the initial episode of erythema nodosum.

History of Exposure to Tuberculosis

Three patients presented evidence of contact with tuberculous patients; only 1 of these showed slight enlargement and calcification of the hilar lymph nodes. Five patients entered the hospital with histories suggestive of possible contact with tuberculosis, 3 of whom roentgenologically showed intrathoracic abnormalities.

*O.T. (old tuberculin) is used for these tests; in children and in adults in whom tuberculosis is suspected, the initial dilution is 1:100,000, and in other adults, 1:10,000; a test is not reported "negative" until a 1:1000 dilution has been employed.

Communicability

Two employees of the Mount Sinai Hospital who were roommates developed erythema nodosum lesions five days apart. In both, there was a history of an upper respiratory infection preceding the eruption.

Biopsy

Biopsies were performed in 10 of the 88 cases of erythema nodosum. Specimens were taken from the skin in 8 cases and from lymph nodes in the axilla in 2. The microscopic findings in the skin sections in all cases were those of erythema nodosum. In 1 case with concomitant lymphadenopathy, an axillary lymph node that was removed showed nonspecific hyperplasia. The lymph node removed from a patient with an axillary abscess of a few months' duration showed nodular areas with small central abscesses. Epithelioid cells were seen, but no tubercle bacilli were present.

Subsequent Case Records

Thirty-four patients returned for follow-up examinations. One patient subsequently showed questionable evidence of rheumatic heart disease, and another returned seven years later with an episode of acute rheumatic fever with joint symptoms. Hypertension was noted in 2 patients who reported for examinations following discharge from the hospital. Two others returned with recurrent episodes of eruptions diagnosed as erythema nodosum.

Roentgenologic Features

Chest roentgenograms were available in 56 of the 88 cases. Fourteen of these were associated with pulmonary changes or enlargement of the intrathoracic lymph nodes, or both.

There was roentgenologic evidence of enlargement of mediastinal or lymph nodes, or both, in 12 patients, 3 of whom showed calcification in the nodes.

The hilar shadows were accentuated in 2 cases, and in another there was unusual exaggeration of the pulmonary markings in both upper lobes.

A resolving pneumonic process was noted in 1 case.

In the presence of a clinical diagnosis of childhood tuberculosis, the roentgenogram showed a pneumonic infiltration of the left upper lobe.

A young patient who later died of hematogenous miliary tuberculosis showed nodular infiltrations throughout both lungs.

A thirty-four-year-old woman whose chest roentgenogram revealed fibrocalcific tuberculosis of both upper lobes on several occasions developed episodes of erythema nodosum. The chest findings remained unchanged.

TABLE 2. *Data on Patients with Associated Intrathoracic Changes.*

Case No.	Hospital No.	Date of Admission	Sex	Age	Chest Roentgenogram	Tuberculin Test	Comment	Subsequent Course
				yr.				
1	320304	2/20/30	F	40	2/21/30: moderate enlargement of left hilar lymph nodes.	Not done	Four previous attacks of erythema nodosum during previous 30 years; tonsillitis preceded these attacks.	March, 1931: no recurrence after removal of tonsillar tags.
2	350770	4/8/33	F	9	4/10/33: slight enlargement of hilar lymph nodes, with calcification; calcified primary infection, left base; slight elevation of periosteum on anterior aspect of right tibia beneath soft-tissue swelling of erythema nodosum lesion.	Positive	Mother of patient receiving pneumothorax therapy for pulmonary tuberculosis	1934: another attack of erythema nodosum; chest roentgenogram showed no change.
3	359578	11/23/33	F	5	11/23/33: slightly enlarged hilar nodes, particularly on left side.	Strongly positive	Generalized lymphadenopathy	1938: chest roentgenogram revealed no change; systolic murmur persists; rheumatic heart disease (?).
4	361770	1/20/34	F	30	1/22/34: moderate enlargement of bronchial lymph nodes bilaterally, with slight calcification; resolving left-lower-lobe pneumonia.	Positive	*Systolic* murmur at apex; biopsy of skin on two occasions showed changes consistent with diagnosis of erythema nodosum; intravenous and intramuscular therapy given 10 years previously following two miscarriages; blood Wassermann reaction negative.	4/2/34: no complaints.
5	364252	3/30/34	F	29	4/4/34: right bronchial and paratracheal lymph nodes enlarged.	Not done	Cervical lymph nodes palpable; sister died of tuberculosis 25 years previously.	Patient failed to report for follow-up.
6	366529	5/23/34	F	13	5/2534: calcified lymph nodes at both lung roots; prominence of pulmonary conus.	Positive	Bilateral submandibular and axillary adenopathy; systolic murmur at base (rheumatic heart disease?); electrocardiogram normal.	Patient failed to report for follow-up.
7	375748	1/17/35	M	9	1/19/35: pneumonic infiltration extending from left hilum to periphery of lung in midportion of left upper lobe; enlarged left hilar nodes.	Strongly positive	Bilateral cervical and epitrochlear lymphadenopathy; clinical diagnosis: childhood pulmonary tuberculosis.	1/31/35: chest roentgenogram showed moderate decrease of pneumonic infiltration in left upper lobe; no subsequent record.
8	378461	4/5/35	M	13	4/6/35: unusual exaggeration of pulmonary markings of both upper lobes.	Positive	Systolic and presystolic murmur (rheumatic heart disease)	1941: no cardiac murmurs.
9	412329	8/3/37	F	25	8/4/37: left hilar lymph nodes enlarged.	Positive	Chest roentgenogram of patient's father showed evidence of old and questionable recent tuberculosis	November, 1937: pain in region of left upper lobe, with slight fever four weeks previously.
10	421390	3/14/38	F	16	3/17/38: lateral roentgenogram showed enlarged tracheobronchial lymph nodes; prominent pulmonary conus.	Positive	Cervical adenitis; systolic murmur at apex; 1933: attack of erythema nodosum.	June, 1939: occasional athralgias; heart normal.
11	433021	12/3/38	M	6	12/6/38: widening superior mediastinum bilaterally due to enlarged nodes; exaggerated pulmonary markings, somewhat nodular in character, particularly on right side; 12/24/38: widespread nodular infiltrations bilaterally; nodes enlarged; 1/11/39: no essential change.	Strongly positive	Rachitic chest deformity; spleen palpable; clinical diagnosis: miliary tuberculosis.	Death at Seaview Hospital on August 3, 1939; post-mortem findings: diffuse hematogenous miliary tuberculosis; lungs showed miliary tuberculosis, and the enlarged hilar and mediastinal lymph nodes revealed caseous tuberculosis.
12	453063	2/28/40	F	25	3/7/40: hilar shadows accentuated on both sides; moderate enlargement of mediastinal and hilar lymph nodes.	Negative	Residual strabismus from attack of "meningitis" at age of 2	2/3/41: almost complete regression of previous chest findings.
13	476893	7/28/41	F	32	8/1/41: distinct exaggeration of right hilar shadows and slight widening of superior mediastinum to the right; appearance most likely due to enlarged hilar and paratracheal lymph nodes.	Strongly positive	Skin biopsy: not reported; past history: "water on kidney" 10 years previously.	November, 1941: patient recently admitted to another hospital with hydronephrosis and hypertension.
14	374634	5/7/41	F	34	5/21/41: fibrocalcific foci in both upper lobes; no definite recent infiltration.	Strongly positive	Skin biopsy showed changes due to erythema nodosum.	November, 1941: patient subsequently developed new crops of erythema nodosum on three occasions in previous 5 months.

Table 2 presents a more detailed analysis of the 14 patients with intrathoracic changes.

In view of these findings, it is obvious that roentgenologic examination of the chest should be performed in all cases of erythema nodosum, even in the absence of chest complaints. Examination of the chest in the lateral position should be included. In our experience, in the 1 case in which a roentgenogram in this position was available, an enlarged lymph node was demonstrated, although the routine posteroanterior film failed to reveal it. It is probable that had the chests been examined in both positions routinely, more cases with enlarged intrathoracic nodes might have been discovered. In questionable cases of enlargement of the intrathoracic lymph nodes, more information may be secured by fluoroscopy and sectional radiography, and perhaps also by kymography.

Summary and Conclusions

A survey of 88 cases of erythema nodosum indicates that the condition may be found during the course of various diseases, both infectious and noninfectious, virus, bacterial, chemical and toxic. It is evident that no common agent causes these diseases that might be expected to be the cause of erythema nodosum. In a small group of patients (approximately 15 per cent), no evident associated disease was present.

The following conditions were associated with the erythema nodosum in these 88 cases: tuberculosis (4 cases); rheumatic heart disease (7 definite and 10 questionable cases); ulcerative colitis (6 cases); upper respiratory infections (49 cases); arthralgias (28 cases); drug ingestion (8 cases); inactive syphilis (4 cases); gonorrhea (4 cases); herpes zoster (1 case); measles and otitis media (1 case); eye disease (1 case); prostatic abscess (1 case); postoperative infection of abdominal wall (1 case); axillary abscess (1 case); and peritonsillar abscess (1 case).

Fourteen of fifty-five available chest roentgenograms revealed positive intrathoracic findings. Twelve showed slight to moderate enlargement of the nodes, three with calcification. Pulmonary abnormalities were noted in 5 cases — resolving pneumonic process, pneumonic infiltration, exaggerated pulmonic markings, miliary tuberculosis and fibrocalcific tuberculosis. Tuberculin tests, which were performed in 12 of the 14 patients, were positive in 11.

The patients whose roentgenograms showed intrathoracic adenopathy or pulmonary infiltration, or both, had associated disease of the respiratory tract that could account for the abnormalities and often obviously did. In the cases in which the development of erythema nodosum was associated with ulcerative colitis, prostatic abscess, peritonsillar abscess, rheumatic heart disease, gonorrhea, conjunctivitis, postoperative infection, axillary abscess, measles and otitis media, and ingestion of drugs, the chest roentgenograms failed to demonstrate any pulmonary changes or intrathoracic lymphadenopathy.

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A PRACTICAL OUTLINE FOR THE TREATMENT OF BURNS*

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FOR several years before the present war, the number of people in this country who died each year from burns ranged in the vicinity of 6000. In addition, 1500 died each year as a result of conflagration, and untold thousands lived but were permanently disfigured or deformed. Since burns are not acquired or inherited like disease, but are almost always purely accidental, more and more rigid safety measures have been instituted both in the home and in industry in an attempt to reduce these figures. Obviously, if fewer people were burned, there would be fewer deaths, but prevention is only one of the two significant factors concerned in this high death rate. The other, equally important, factor is a proper appreciation of how to handle the burned patient from a medical standpoint. To lessen the incidence of confused, unintelligent and inadequate care by the layman, nurse and physician alike would effect an appreciable reduction in the number of fatalities and deformities caused by burns.

During peacetime, 83 per cent of all burns occur in the home, 10 per cent in industry, and 7 per cent in public accidents. It is obvious from these figures that there is a great need for both an educational program and the elimination of physical hazards in every home. This is to be kept in mind now and after the war is over. However, in wartime, with the possibility that explosive and incendiary bombs will drop on civilian rather than on military lines of defense, the number of burn casualties is in danger of being greatly increased. This has been true in every country that has experienced any number of air raids. For this reason, every person should have some knowledge of what to do and, perhaps more vital, what *not* to do for a person who has been burned.

The Red Cross and the Office of Civilian Defense have accepted and are discharging a tremendous responsibility in training a large number of laymen in the rudiments of first aid. Every physician in the country has also been preparing and refreshing his mind, so that he will be equipped to take care of war casualties.

In line with this general preparation, the following condensed outline for the treatment of burns has been drawn up, based on experience both personal and collective, to aid in the rapid assimilation of the present knowledge on this subject.

I. THERMAL BURNS (HOT LIQUIDS, STEAM, FLAME AND HOT METALS)

1. First-Aid Instructions for Laymen.

a. Treat all burned patients for shock.

b. If a physician is not present but is available:

(1) Cover small burns with a clean cloth or sterile bandage, and take the patient to the first-aid post.

(2) For extensive burns, cover the patient with a clean sheet and blankets; bring the doctor to the patient, if possible — otherwise send the victim to a hospital immediately.

(3) Do *not* put tannic acid ointment on any burn.

c. If a physician is neither present nor available and it seems likely that one or two hours may elapse before the patient can be seen by a physician:

(1) For small burns, clean the area by gently washing with a mild soap under running water — if running water is not available, do not clean, but cover the burn with a paste of sodium bicarbonate and water; wrap the burned area securely in clean or sterile cloths, and send the patient to a physician.

(2) For extensive burns, remove the clothing but do not try to clean the area; cover the burned parts with clean cloths (napkins, pillow cases or sheets) soaked in a warm solution of sodium bicarbonate — cover with dry cloths; keep the patient warm and get him to a hospital as soon as possible; give strong coffee or tea by mouth.

d. Important points to be remembered:

(1) Do *not* apply tannic acid jelly or strong tea to a burn until after the burn has been properly cleaned by a doctor.

(2) Do *not* apply grease in any form.

(3) Do *not* move the patient about in an attempt to put on a neat bandage; disturb him as little as possible.

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2. First-Aid Instruction for Physicians.

a. Check all patients with minor or major burns for shock; treat this even before the burned area is examined.

b. Give morphine liberally: administer a dose double that which would normally be used for the patient if he were to have a preoperative dose for an elective operation.

c. If shock is severe, administer oxygen by mask or tube and give caffeine intramuscularly; if plasma is available, give 5 cc. per pound of estimated body weight intravenously; if plasma is not available, give physiologic saline solution — 10 cc. per pound of body weight — while plasma is being obtained.

d. When shock has been effectively combated, carefully remove the bandages and clothes; examine the burn and try to estimate extent and depth of the burn.

e. If the burn is minor:

(1) Cleanse thoroughly by washing gently for about seven minutes with sponges soaked in 50 per cent green soap (solution, not tincture) and 50 per cent hydrogen peroxide.

(2) Break all blisters, and remove all dead skin and debris (use sterile instruments).

(3) Flush with copious amounts of physiologic saline solution, or distilled water, and dab dry.

(4) Dust the area with sulfathiazole, sulfadiazine or sulfanilamide powder.

(5) For burns of the hands, feet, face and genitalia, apply a sterile ointment and cover as well as possible with sterile gauze and bandage.

(6) For burns elsewhere on the body tannic acid jelly or triple-dye jelly may be used; cover with sterile gauze, apply an Ace bandage, and splint the part involved.

f. If the burn is major:

(1) Remove the clothes sticking to the burn and gross dirt or contamination, but do *not* clean *extensively*.

(2) Dust the area liberally with sulfathiazole, sulfadiazine or sulfanilamide powder (if a 5 per cent sulfadiazine, water-soluble jelly or emulsion is available, this may be used instead of the powder).

(3) If the powders are used, cover the area with a liberal amount of water-soluble glycerin-tragacanth jelly (if this jelly is not available, any sterile ointment or triple-dye jelly can be used; however, the latter are harder to remove when the burn receives its final débridement).

(4) Apply heavy (5 to 7 cm. thick) sterile gauze pads and hold them securely in place under mild pressure with an elastic bandage.

(5) Evacuate the patient to a hospital as quickly as possible.

g. Important points to be emphasized:

(1) Do *not* fail to appreciate the fact that shock must be treated *first* and that examination of the burn should wait until the patient is fairly well recovered from the shock.

(2) Do *not* apply tannic acid in any form until *after* the burn has been *thoroughly* cleansed; never apply it to the hands, face, feet or genitalia.

(3) Do *not* temporize with morphine — give it either in a large enough dose to do some good or not at all.

(4) Do *not* allow the sulfonamide powders to get into the eyes or up the nose (they irritate as foreign bodies).

(5) Do *not* fail to apply a *thick* dressing under mild pressure.

3. Hospital treatment of fresh burns.

a. For minor burns treat the patient as outlined above (Section I, 2*e*, 1–6).

b. For major burns:

(1) Check on the degree of shock still present; administer more morphine, heat and so forth, as required.

(2) If time permits and facilities are available, obtain a red-cell count, hemoglobin determination, hematocrit reading and a serum protein (one or more of these are helpful in determining the degree of hemoconcentration).

(3) Give an initial intravenous infusion of plasma of 3 to 5 cc. per pound of estimated body weight; have more plasma available if it is needed; whole-blood transfusion is not indicated unless there has been appreciable blood loss from some other source; if whole blood is available but no plasma, make an effort to separate the plasma from the red cells by centrifugalization or otherwise.

(4) After shock is well controlled, the patient may need to be anesthetized for proper cleaning; use rectal or intravenous anesthetics for those who may have inhaled hot air or gases.

(5) Wash burned area thoroughly for seven minutes with a mixture of solution of green soap and hydrogen peroxide (equal parts).

(6) Remove all dead skin and debris; use sterile precautions throughout débridement.

(7) Flush thoroughly with physiologic saline solution and, if desired, some mild antiseptic, such as a 1:1000 solution of Zephiran or Merthiolate, or S.T. 37.

(8) For burns of the hands, feet, face and genitalia, dust the area with one of the sulfonamide powders and cover with a sterile ointment (*tulle gras*) and a heavy layer of gauze sponges held in place by an elastic bandage; splint the hands and feet.

(9) For burns elsewhere on the body, the treatment outlined in Section I, 3*b*, 8, *may* be used, provided adequate facilities are at hand to combat fluid loss by repeated plasma transfusions.

(10) For burns elsewhere on the body, the escharotics are *usually* employed, principally 5 per cent tannic acid followed by 10 per cent silver nitrate, the triple dyes or a sulfadiazine spray; whichever method is used, specialized aftercare is required: a clean or sterile electrically heated bed, frequent evaluation of the blood chemical findings, adequate fluid intake enterally and parenterally, and constant nursing and medical appreciation of the problems for each case.

4. Hospital Treatment of Old Burns.

a. If a sulfonamide powder has been used in the first-aid treatment, a débridement as outlined in Section I, 3*b*, 4–7, may be carried out as late as thirty hours after the burn was received.

b. If a sulfonamide has not been used, a complete operative débridement is contraindicated if the burn is eight or more hours old. In this event, the following procedure is advised:

(1) Give shock treatment as outlined in Section I, 3*b*, 1–3.

(2) Immerse the patient in a tub of warm tap water for one or two hours, with constant inflow and outflow of water.

(3) Remove the patient from tub, dab dry and spray with one of the sulfonamide powders.

(4) Either cover the burns with an ointment (preferably *tulle gras*) or use the triple-dye jelly or sulfadiazine spray; do *not* use tannic acid in any form.

(5) As an alternative to the procedure outlined immediately above, one may use dressings wet with physiologic saline solution, a Bunyan envelope or *tulle gras* with Eusol (12.5 gm. chlorinated lime, 12.5 gm. boric acid and 1000 cc. distilled water—let the mixture stand twenty-four hours, then filter and keep in a tightly corked bottle); if the burn is coated heavily with fibrin and pus, one of the latter is preferable *first*, to be followed later by a sulfonamide powder.

c. In second-degree burns, healing takes place without grafting over a period of ten days to two weeks.

d. In either superficial or deep third-degree burns (so-called "third-degree," "fourth-degree" and "fifth-degree," according to one system of classification), grafting may be necessary, depending on the extent and site involved.

e. If grafting is necessary, certain precautions must be observed before proceeding:

(1) The patient must be free from infection, in good health and with a normal red-cell count.

(2) An estimate of the amount of tissue to be replaced must be made, and a program outlined for its transfer.

(3) The granulations must be flat, firm and cherry pink.

(4) The granulations should be removed down to the fibrous-tissue base from which they spring, and depending on the site involved, this fibrous base may also be removed.

(5) For defects involving the loss of skin only, a thin or thick razor graft (Thiersch or split Thiersch) is preferable.

(6) For small areas involving the skin of the face or hands, a full-thickness graft (Wolfe or Wolfe-Krause) may be used interchangeably with the thick razor graft.

(7) For areas involving the loss of both the skin and subcutaneous tissue, a single-hinged or double-hinged pedicle flap (pedicle, gauntlet, tube or rope) must be used.

(8) Bone, cartilage and fascia may also be replaced, but this is usually done six to eight months after the skin defects have healed.

(9) Do *not* use island grafts (pinch, Reverdin, small deep and Davis grafts) unless

nothing else is possible; there is seldom occasion for their use.

II. Chemical Burns

(Whoever treats chemical burns should take adequate precautions to protect himself.)

1. Mustard Gas.

a. First aid for exposure to mustard-gas vapor (one to eight hours).

(1) Remove and place all clothes in decontamination bucket.

(2) Give a thorough soap-and-water bath, including shaving or clipping short of all hair and rewashing these areas.

(3) Apply a bleaching-powder wash, followed by a second soap-and-water cleansing.

(4) Keep the patient under observation for twelve hours; if there is no rash or blisters at the end of that time, the patient may be discharged.

b. Late treatment for exposure to mustard-gas vapor (eight hours and over):

(1) Treat the patient for shock; rash and blisters have appeared over warmed areas of the body (axilla, groin and so forth), with severe itching and beginning shock.

(2) Do *not* sedate heavily with morphine (pulmonary complications due to inhalation of the gas may be increased by a lowered respiratory rate).

(3) Anesthetize by the rectal or intravenous route, if necessary.

(4) Clean the burn thoroughly, as outlined in Section I, 3*b*, 5–7.

(5) Apply *tulle gras* over all raw surfaces and follow with a heavy dressing wet with equal parts of Eusol and mineral oil.

(6) Apply a heavy dressing, held in place with gauze and an Ace bandage under mild pressure.

(7) Follow the routine outlined for the aftercare of second-degree or third-degree thermal burns (Section I, 4*e*, 1–9).

(8) For very late infected cases seen two or three days after exposure, follow the routine outlined in Section I, 4*b*, 1–3, 5.

c. First aid for contact with mustard-gas liquid.

(1) Within five minutes, *blot* off excess mustard gas by dabbing with dry pads.

(2) Dab the area gently and repeatedly with pads moistened in kerosene, gasoline or alcohol; wring the pads out so that excess liquid will not drip on the patient and spread the burn.

(3) Thoroughly wash the entire area with a mixture containing equal parts of green soap and peroxide.

(4) Wash the area again with alcohol.

(5) Dry by blotting, and apply a dry dressing that is to be removed and the area examined every two hours for the next twelve hours; if the area looks normal at the end of twelve hours, the patient may be discharged.

d. Late treatment for contact with mustard-gas liquid.

(1) If blisters have formed, dab with pads of kerosene gently to get rid of excess liquid; do *not* use a bleaching agent.

(2) There is no need to sedate heavily or anesthetize (the area is usually painless after liquid has penetrated through the skin).

(3) Carry out full débridement as outlined in Section I, 3*b*, 5–7, and follow with a *tulle gras* and Eusol dressing.

(4) In very late cases when the blisters have broken and have become infected, carry out the routine outlined in Section I, 4*b*, 2, 3, 5.

(5) In the late cases, as soon as the fibrinous infected coat has been removed from the raw surfaces by the Eusol, the sulfonamides may be used.

(6) Late care, including grafting, is the same as that for thermal burns.

2. Lewisite.

a. First aid for exposure to lewisite vapor.

(1) Remove clothing at once.

(2) Wash entire body with hydrogen peroxide; follow this with a complete and thorough bath with soap and water and an alcohol sponging.

(3) Keep the patient under observation for 12 hours; if no blisters appear, he may be discharged.

b. Late treatment for exposure to lewisite vapor.

(1) Sedate and give a rectal or intravenous anesthetic if burns are extensive.

(2) Wash around and over each blister with soap and hydrogen peroxide; be very gentle.

(3) Break the blister, being very careful to catch all the blister fluid on a sponge (throw sponge in decontamination bucket); immediately apply a pad wet with hydrogen peroxide to the raw area; renew this pad frequently.

(4) After all blisters have been broken and covered with a pad of hydrogen peroxide, carry out full operative débridement as outlined in Section I, 3*b*, 5–7.

(5) Cover the burn with a *tulle gras* and Eusol dressing, thick gauze and an Ace bandage.

(6) If the burn remains clean, reapply the dressing described in Section II, 2*b*, 5, each day.

(7) If the burn becomes infected, the treatment is the same as that outlined in Section I, 4*b*, 2, 3, 5.

c. First aid for exposure to lewisite liquid.

(1) Within one minute after exposure remove the clothes and start treatment.

(2) Swab area with hydrogen peroxide repeatedly for thirty minutes.

(3) Wash with soap and water for seven minutes, and follow with an alcohol pad, which is left in place for five minutes.

(4) Pat dry, and apply a dry dressing; if no blisters have formed at the end of twelve hours, the patient may be discharged; if blisters have formed, carry out the routine outlined in Section II, 2*b*, 2–4, except that anesthesia is usually not necessary.

d. Late treatment for exposure to lewisite liquid.

(1) If an unbroken blister is found, carry out the routine outlined in Section II, 2*b*, 1–7.

(2) If the blister has broken and the patient shows signs of arsenical poisoning, excise entire area under anesthesia at once, and follow by grafting as outlined in Section I, 4*e*, 5–8.

(3) If the area is too extensive for excision and is grossly infected, the prognosis is poor; however, treat the patient as outlined in Section I, 4*b*, 2, 3, 5 and attempt to control the arsenical poisoning by intravenous sodium thiosulfate.

3. Phosphorus.

a. If there is no phosphorus that is still burning in or on the skin, treat the burn as a thermal one (Section I).

b. If bits of phosphorus that are still smouldering lie on or in the skin:

(1) Wet the area and keep it wet with anything, but preferably warm water (this melts and stops further burning of the particles; if the area becomes dry, the particles will begin to burn again).

(2) If a 5 to 15 per cent solution of copper sulfate is available, apply this at once (burning is stopped temporarily).

(3) No matter which of the above methods is used, squeeze or pick out the phosphorus particles with forceps and then treat as any thermal burn.

4. Acids and Alkalies.

a. Remove the patient's clothing at once, taking care that the chemical agent does not burn others.

b. Flush area under cold running water (the heat of dilution of strong chemicals is carried away by the continuous washing); if running water is not available, douse the patient in a tank, tub, or lake; if the burn is due to lime, brush off the excess before wetting.

c. Do not attempt to neutralize the burning agent (the heat of reaction may cause a deeper burn, or the neutralizing agent itself may burn).

d. After removal of the burning agent, treat as a thermal burn (Section I).

III. Electrical Burns

1. General Effects.

a. Do *not* touch a patient who is still in contact with the electric current, unless proper insulation is possible.

b. Never regard a recently shocked person as dead, even if the heart beat cannot be heard.

c. Continue artificial respiration, oxygen and cardiac stimulants until rigor mortis sets in (several patients have recovered after having been apparently dead for hours).

2. Local Effects.

a. Except for a very few cases almost all electrical burns are of third degree, owing to the intense heat and the coagulation of blood in the vessels supplying the area involved.

b. Do *not* be misled by the apparently innocuous appearance of the fresh electrical burn; institute treatment at once:

(1) Sedation or anesthesia is rarely necessary.

(2) Clean the area thoroughly with a mixture of green soap and hydrogen peroxide and flush with saline.

(3) Apply a sterile ointment, gauze and an elastic bandage; splint the part involved.

(4) Do *not* apply any substance that will form an eschar.

(5) Apply daily dressings under strict aseptic precautions so that the amount of late necrosis and slough may be observed.

(6) Do *not* cut away sloughing tissue; allow the demarcation and detachment of dead tissue to take place without surgical aid (hasty operative removal may result in excision of tissue that will be viable and necessary for repair).

(7) Vessel walls are damaged, so that secondary hemorrhage is frequent; have a sterile tray with hemostats and a tourniquet always at the bedside.

(8) After the slough has disappeared, treat as in Section I, 4*e*, 5–8.

A general survey of the treatment of burns has been outlined, with particular emphasis on the treatment of shock, the need for gentleness in the handling of tissues and the necessity for a complete cleansing of the burned area before medicaments are applied. Each burn presents an individual problem; consequently, it is impossible to outline specific details for every possible type of burn. The broad general principles have been stressed, in addition to specific instructions that, if followed within reason, will cause an appreciable reduction in the number of fatalities.

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MEBARAL IN THE TREATMENT OF EPILEPSY*

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IN 1929, the drug known in this country as Mebaral was introduced in Europe under the name of Prominal, the chemical formula being n-methylethyl-phenyl barbituric acid. It has been utilized in Europe quite extensively, but its introduction in the United States is recent, so that it is not sufficiently known to the medical profession in this country. Mebaral is supplied in tablets of 0.03 gm. (½ gr.) and 0.2 gm. (3 gr.) on the erroneous supposition that it is half as potent in sedative qualities as phenobarbital, to which it is closely related chemically. In general, it may be stated that its sedative effect is about one third that of phenobarbital.

In 1932, Weese[1] pointed out that the spans between the hypnotic, narcotic and lethal doses of Mebaral are greater than those of phenobarbital, that is, the margin of safety is greater. In the same year, Blum[2] reported that he had tried Mebaral for three years on several hundred epileptic patients in his hospital and private practice. He found that 0.2 gm. (3 gr.) two or three times a day decreased the epileptic seizures about 50 per cent. He found it valuable in petit mal as well, and observed no hypnotic effects. Heyde[3] considered Mebaral slightly superior to phenobarbital as an anticonvulsant, but greatly superior in the treatment of psychic symptoms in epilepsy. He favored it for the treatment of ambulatory and noninstitutional patients.

Plaut,[4] in 1935, stated that the drug was very useful as a sedative, his material being 60 patients suffering from insomnia, nocturnal enuresis, hyperthyroidism and various psychoses. Using it in dosages of 0.1 to 0.2 gm. (1½ to 3 gr.) a day, he found no serious by-effects and noted that employed patients were not incapacitated by drowsiness.

Page,[5] in 1936, compared his findings with Mebaral and phenobarbital during equal five-month periods. In the period under phenobarbital administration, the patients had a total of four hundred and seventy-six grand-mal seizures. In the second period, under the influence of Mebaral, the same patients had two hundred and forty-four grand-mal attacks. Page also noted that under Mebaral the patients were bright and cheerful, and could care for themselves.

Henderson,[6] in 1937, selected 13 patients with grand-mal epilepsy who had not shown sufficient improvement on clinical trial with other drugs, and, during a period of twelve months' administration with Mebaral, noted a two-thirds reduction in the number of attacks as compared with those in the previous period. He found that 0.6 gm. (9 gr.) a day was apt to cause drowsiness, and believed that the optimum clinical effects were obtained with 0.4 gm. (6 gr.) a day. His patients did not suffer from gastrointestinal disturbances, urinary changes, or significant fluctuations in blood pressure, and they did not develop a tolerance that required increased dosage. In a few

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cases of petit-mal epilepsy, he was not able to produce favorable changes.

Millman[7], in the same year, reviewed the comparative findings in 39 patients previously on phenobarbital whose medication had been changed to Mebaral with a gradual increase in dosage 50 per cent greater than that of phenobarbital. There was a great reduction in both grand-mal and petit-mal attacks, the average reduction being slightly less than two thirds. Of 27 patients who showed abnormal behavior and were considered to be epileptic equivalents, or psychic manifestations, there was improvement in 19. Many of the adults were given 0.6 gm. (9 gr.) a day for two years, without ill effects. In children, he employed the formula, age ÷ age + 12, to determine the fraction of the adult dose that they should receive. In a few adults receiving maximum dosage, he noted drowsiness, which disappeared when the drug was withheld for a few days.

Our own experience with this drug is threefold. Concerning its value in agitated, depressed and anxiety states, about which we shall report at a later date, it suffices to say that this drug seems to us to be by far the best sedative in the treatment of these conditions, since it produces more tranquillity and less narcosis than any other drug, and without untoward symptoms unless given in doses above 0.4 to 0.6 gm. (6 to 9 gr.) a day. Secondly, since the treatment of epileptics in private and outpatient practice is not methodically controlled, it cannot be analyzed well. The impression of both of us is that this drug is efficacious in the treatment of epilepsy, of both the grand-mal and the petit-mal types, and that it has fewer undesired effects than either phenobarbital or Dilantin, its chief rivals in the treatment of epilepsy. The third group consists of controlled epileptic patients at the Grafton State Hospital, with which this paper is mainly concerned.

The last group has been known to us for years and represents a group relatively refractory to other drugs. The rate of convulsive expectation had been established over periods of six months to three years of observation. These patients had had previous treatment in this hospital with phenobarbital alone, and with phenobarbital and Dilantin; we here record the experimental treatment with Dilantin and Mebaral, and with Mebaral alone. The comparison is made between the effects of the former two drugs and those of Mebaral on the incidence of epileptic attacks in these patients as compared with the effects of previous drugs used. We are thus not comparing the effects of Mebaral on cases easily controlled by phenobarbital or Dilantin, or by phenobarbital and Dilantin, but on patients who had not done well on these drugs.

The results of our investigations in these relatively refractory patients may be stated as follows. Of 12 patients who had trial treatment separately with phenobarbital and with Mebaral, 2 did better with the former, and 10 with the latter. On Mebaral alone, there were 42 per cent fewer seizures than with phenobarbital. Nine patients had separate trials of phenobarbital and Dilantin and of Mebaral alone. Two did better with the former, and 7 with the latter. On Mebaral alone, there were 48 per cent fewer seizures than with phenobarbital and Dilantin. Eleven patients had separate trials with a combination of Dilantin and Mebaral and with Mebaral alone. Four did better on the latter, and 7 on the former. There were 38 per cent fewer seizures on Mebaral alone.

The average period for any treatment ranged from twenty-seven weeks to one year. We considered these periods sufficient for determining the value of any drug or set of drugs in patients having frequent attacks.

TABLE 1. *Comparative Effects of Desultory Preliminary Medication and Concentrated Individualized Therapy with Phenobarbital, Phenobarbital and Dilantin, Dilantin and Mebaral, and Mebaral.*

	AVERAGE NUMBER OF SEIZURES PER TEN WEEKS				
PATIENT	INADEQUATE PHENOBARBITAL THERAPY	ADEQUATE PHENOBARBITAL THERAPY (56 WEEKS' AVERAGE)	PHENOBARBITAL AND DILANTIN THERAPY (23 WEEKS' AVERAGE)	DILANTIN AND MEBARAL THERAPY (25 WEEKS' AVERAGE)	MEBARAL THERAPY (52 WEEKS' AVERAGE)
F. McQ.	53	—	—	5	5
E. C.	27	6	5	1	2
B. P.	12	4	5	2	3
M. McC.	13	2	—	1	1
C. R.	14	5	—	3	4
N. S.	8	7	6	—	1
M. W.	23	14	16	13	3
M. Hy.	6	5	10	9	6
M. Hn.	8	8	5	4	4
C. C.	19	3	3	3	3
E. H.	18	8	8	16	11
M. H.	11	—	9	12	4
W. L.	9	2	1	—	1

The dosage of phenobarbital given alone was from 0.13 to 0.45 gm. (2 to 7 gr.) per day, the average being 0.27 gm. (4 gr.). When phenobarbital was combined with Dilantin Sodium, the dosage of the former remained unchanged, and 0.2 to 0.4 gm. (3 to 6 gr.) of the latter was added, the average dose of this drug being 0.3 gm. (4½ gr.). When Dilantin and Mebaral* were used, the daily dose of the former ranged from 0.2 to 0.3 gm. (3 to 4½ gr.) a day, the average being 0.25 gm. (3½ gr.) and that of the latter averaged about 0.6 gm. (9 gr.). When Mebaral was used alone, the dose was from 0.4 to 0.8 gm. (6 to 12 gr.) a day, the average being 0.6 gm. (9 gr.).

*Kindly supplied by the Department of Medical Research, Winthrop Chemical Company, New York City.

In Table 1, the column labeled "inadequate phenobarbital therapy" indicates the former incidence of seizures during each ten weeks for periods ranging from six to twenty-four months immediately preceding the institution of the program of intensive individualized therapy, which has been described in a previous paper.[8] That phenobarbital cannot be discredited is evidenced by the fact that this drug alone in adequate amounts reduced the number of seizures 66 per cent from that obtained by desultory treatment.

In a few patients, Mebaral produced drowsiness and gait disturbance, similar to the effects of phenobarbital, although they were less marked and more easily dissipated. We found that amphetamine (Benzedrine) sulfate, in doses of 10 to 20 mg. by mouth, was equally useful in such cases as a therapeutic agent pending the improvement that invariably attended reduction of dosage of Mebaral and rest in bed. In general, such toxic symptoms attended the use of Mebaral much less frequently than the use of phenobarbital, despite the use of proportionately higher dosage.

Summary and Conclusions

Attention is called to the value of Mebaral (n-methylethyl-phenyl barbituric acid) in the treatment of epilepsy.

The drug is particularly useful for epileptic children, who prefer tasteless medication, for psychotic epileptics who must be treated by medication concealed in their food, for patients who cannot be given adequate phenobarbital because of toxic drowsiness and, finally, for trial in patients who do not show satisfactory response after trials of phenobarbital, Dilantin and bromides, separately or in combination.

In certain cases relatively refractory to other medication, significant improvement was noted when Mebaral was utilized.

Mebaral was found to be less productive of toxic symptoms than phenobarbital or Dilantin, and proportionately higher dosage was continued with safety and as great or greater clinical effectiveness.

In the private practice of one of us (A.M.), Mebaral has become the drug of first choice for the treatment and control of grand mal and petit mal. In cases in which it does not work well by itself, it combines very well with Dilantin. In those cases in which it is not effective, it is discarded, and phenobarbital and Dilantin in combination are used.

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HYPOCHROMIC ANEMIA WITH KOILONYCHIA (SPOON NAILS)*

Report of a Case

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KOILONYCHIA (spoon nails), an interesting abnormality, is particularly noted in chronic hypochromic anemia. In the case reported below, koilonychia appeared twice during recurring episodes of hypochromic anemia, disappearing each time after successful treatment of the anemia with iron. Hypochromic anemia is due to iron deficiency, which is essentially dependent on chronic blood loss. Women require about four times as much iron until the menopause as men do, so that hypochromic anemia and, consequently, koilonychia are relatively commoner in women.

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Case Report

First admission. A 46-year-old widowed painter and decorator, who had come to the United States from Glasgow at the age of 22, was admitted to the hospital on January 5, 1934, because of gradually increasing shortness of breath, palpitation and mild ankle edema. Three weeks before admission, he noted substernal tightness on exertion. There was no history of weight loss or melena.

Examination showed a middle-aged man with pallor of the skin, a beefy red tongue, slight pitting edema of the ankles and spooning of the nails. The heart was enlarged, and the blood pressure was 110/60.

Examination of the blood showed a red-cell count of 2,300,000 with a hemoglobin of 20 per cent, and a white-cell count of 6000 with 70 per cent polymorphonuclears, 20 per cent lymphocytes and 10 per cent mononuclears. Red cells in the smear showed marked hypochromia, microcytosis and variation in size and shape. There was only a rare

immature cell, and the platelets appeared normal in number. Gastric analysis showed no free acid, fasting or after histamine. The total acidity was 12 units. Six stools were guaiac negative. The nonprotein nitrogen was 31 mg. per 100 cc.

The patient was given iron and ammonium citrates, 90 gr. a day. The reticulocytes reached 6.7 per cent on the 7th day, and the red-cell count rose to 4,000,000 and the hemoglobin to 72 per cent 5 weeks later, when he was discharged.

Following discharge, the patient was well and continued to work as a painter for 6 years, without symptoms suggesting either anemia or lead poisoning. He took iron pills intermittently. He continued to be extremely careful about the handling of lead paint, and since he is an intelligent man, it is likely that his exposure to this toxic substance was minimal for a painter, although he had followed this trade since the age of 15. About a year following discharge, the spooning of the nails disappeared.

Second admission (February 20, 1941). The patient had remained essentially well until 6 months before entry, when there was an insidious onset of easy fatigue, weakness, shortness of breath and increasing pallor, with development again of spooning of the nails. He had very slight ankle edema, but no tingling or numbness of the extremities, soreness of the tongue, gastrointestinal complaints or weight loss. The diet had apparently been adequate. For the preceding 5 or 6 years, however, the patient had noticed very occasional streaking of the stools with bright-red blood.

Examination showed a well-developed and well-nourished but very pale man in no distress. The skin had a slightly yellow tint, but the scleras were clear. The tongue was pale, with slight atrophy along the margins. The heart was slightly enlarged on x-ray and physical examination, with a harsh systolic murmur at the apex and base. The blood pressure was 115/60. The spleen was palpable at the left costal margin, but the liver was not felt. There was no edema of the extremities. Spoon-like concavity of the fingernails was marked (Fig. 1), with cracked margins but no longitudinal striations. Rectal examination revealed skin tabs at the anus and moderate-sized internal hemorrhoids with several bleeding points. Proctoscopy on three occasions showed no rectal ulceration, neoplasm or polyp. X-ray examinations of the colon and upper gastrointestinal tract were entirely negative. The reflexes were physiologic, and vibration and position sense normal.

On admission, the red-cell count was 2,860,000 with a hemoglobin of 22 per cent and a hematocrit of 19 per cent; the mean corpuscular volume was 65 cubic microns, the mean cell hemoglobin concentration 24 per cent, and the mean corpuscular hemoglobin 16 micromicrograms, indicating severe hypochromic anemia. The white-cell count was 4100, with 72 per cent polymorphonuclears, 19 per cent lymphocytes, 8 per cent monocytes and 1 per cent eosinophils. The red cells showed hypochromia and variation in size and shape; 0.4 per cent reticulocytes were present on admission, and platelets were reduced in the smear. At no time were any stipple cells suggestive of lead poisoning seen. Gastric analysis showed a free acid of 0, a total acid of 4 units and, after histamine, a free acid of 5 units, and a total acid of 10 units. Sixteen stools were guaiac negative; one showed a blood-streaked exterior and was guaiac positive. The icteric index was 4. Liver-function studies, including hippuric acid excretion and urobilinogen determinations, were normal. The total protein was 6.3 gm. and the nonprotein nitrogen 27 mg. per 100 cc.

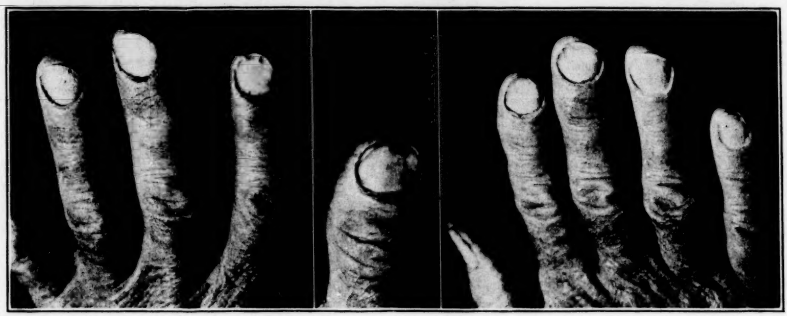

FIGURE 1. *Nails of the Patient before Treatment.*

The patient was given ferrous sulfate, 16 gr. a day, supplemented with dilute hydrochloric acid and a high-vitamin, high-calorie diet. While in the hospital, he was entirely asymptomatic, and showed progressive increase in strength and loss of pallor.

The highest reticulocyte count was 2.8 per cent, but the red-cell count and hemoglobin showed a rapid and steady rise until 5 weeks after admission, when the red-cell count was 5,250,000, the hemoglobin 91 per cent, the hematocrit 43 per cent, the mean corpuscular volume 84 cubic microns, the mean corpuscular hemoglobin concentration 27 per cent and the mean corpuscular hemoglobin 22 micromicrograms. After the 1st week, the white-cell count rose to levels between 6100 and 13,700. Gastric analysis 4 weeks after admission showed free acid of 8 units and total acid of 56 units; after histamine, the free acid was 18 and the total acid 60 units.

The patient was transferred to the Surgical Service, where three internal and external hemorrhoids were excised, and discharged 6 weeks after admission.

The patient returned to work, taking iron for several

months following discharge. Eight months after discharge, he was entirely well, and the nails had returned to their normal convex contours (Fig. 2). Examination of the blood showed a red-cell count of 5,260,000 with a hemoglobin of 99 per cent, a hematocrit of 46 per cent, a mean corpuscular volume of 88 cubic microns, a mean corpuscular hemoglobin concentration of 33 per cent and a mean corpuscular hemoglobin of 29 micromicrograms, and a white-cell count of 6800.

Comment. The patient gradually developed severe hypochromic anemia coincidentally with koilonychia. On adequate doses of iron, the anemia and koilonychia disappeared, and while taking iron only intermittently, he continued to be well until 6 years later, when anemia and koilonychia again began to develop. Again, these were cured by treatment with iron. Hemorrhoids, thought to be the source of chronic blood loss and thus of the iron deficiency, were removed after the second episode of anemia.

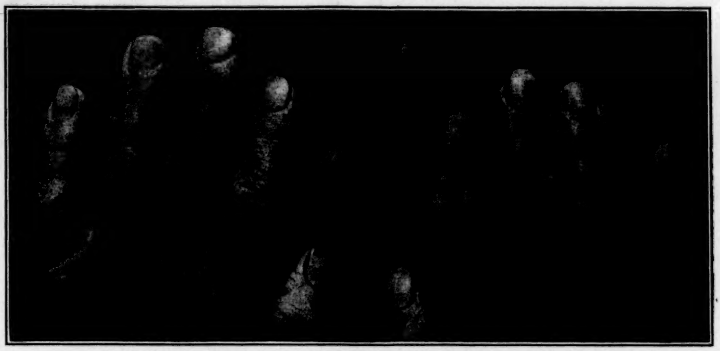

FIGURE 2. *Nails of the Patient Fourteen Months after Treatment Had Been Started.*

DISCUSSION

Koilonychia (κοῖλος, hollow; ὄνυξ, nail) is characterized by an everted distal edge, flat lateral margins, and a spoonlike central concavity of the fingernail. Any number of fingers may be affected and in varying degrees. Associated changes commonly observed are exaggerated longitudinal striations and increased thinness and brittleness of the nails. These changes are also often found in cases of hypochromic anemia lacking typical koilonychia. Flat nails, a less marked phase of koilonychia, have been specially designated "platonychia" by some writers. A case with similar changes in the toenails has been observed by Eddowes (cited by Crocker[1]).

The condition was first described by Ball[2] in 1874, who presented a case to the Society of Biology at Paris, but did not give it a name. Crocker[1] reported another case in 1896, and suggested the name "spoon nails." Heller,[3] in the first edition of his monograph on diseases of the nails (1900), recorded several additional cases and his original case of a "twenty-five year old, rather chlorotic servant girl," and assigned the name "koilonychia" to the deformity. I have been able to find reports of 83 cases in the literature, in addition to the one reported above.

Idiopathic hypochromic anemia became recognized as a distinct entity after Faber,[4] in 1913, called attention to the occurrence of a severe type of chlorosis in middle-aged women with gastric anacidity. Many subsequent observers have noted koilonychia as a frequent but inconstant feature of the disease.

Idiopathic hypochromic anemia (simple achlorhydric anemia, simple achylic anemia, primary hypochromic anemia, achylic chloranemia, chronic chlorosis, chronic microcytic anemia or essential hypochromic anemia) occurs especially but not exclusively in middle-aged women, and is characterized by an insidious onset, long duration, symptoms common to all severe anemias — including paresthesias, but without objective neurologic findings — and, in addition, glossitis and stomatitis. Splenomegaly, koilonychia, cheilitis (fissures at the corners of the mouth) and dysphagia are often present. In the great majority of cases, there is evidence of disturbed gastric secretion (achlorhydria). The anemia is characterized by ready response to adequate iron therapy, and by a tendency to relapse when treatment is discontinued. Careful study often reveals chronic blood loss without adequate iron intake as a cause of the iron deficiency on which the anemia is based. Iron-deficiency anemia has been reviewed by Wintrobe and Beebe,[5] Heath and Patek[6] and others.

There are twelve reports,[1, 7–16] including the present one, comprising a group of 180 cases of idiopathic hypochromic anemia, in which the incidence of koilonychia is stated; it was present in 27 of these cases. In addition, eight observers,[5, 17–23] reporting a total of 365 cases of idiopathic hypochromic anemia, have noted koilonychia in some of the cases under their observation, but have not specified the number in which it occurred.

Flattening, brittleness and exaggerated longitudinal ridging of the nails may be regarded as important signs in cases of idiopathic hypochromic anemia lacking typical koilonychia. Wintrobe and Beebe[5] found marked longitudinal ridging or, less often, koilonychia, in 40 per cent of their 25 cases, and McGeorge[10] found brittle, thin and flexible nails in half of his 23 cases as well as koilonychia in 1. Davies,[8] in a study of 55 cases of hypochromic anemia, found koilonychia in 4, 1 of them a postgastrectomy case, and noted flattening of the nails in 21 and excessive brittleness and tenderness in 31.

Most observers [7–11, 21–25] have remarked that in cases under their observation in which the anemia was successfully treated with iron, the nail changes disappeared. Walderström and Hallen[25] have reported 3 cases of koilonychia without associated anemia, in 2 of which the nails became normal after iron treatment.

The Plummer–Vinson syndrome of anemia, glossitis and dysphagia can probably be regarded as a group of cases having the clinical and hematologic features of idiopathic hypochromic anemia, with dysphagia as a particularly prominent symptom. A large number of cases have been reported, in 27 of which the observers[12, 24–27] made note of the presence or absence of nail changes. Eight of the 27 patients had frank koilonychia. Ahlbom,[28] reviewing 250 cases of carcinoma of the upper gastrointestinal tract, noted frequent appearance of hypochromic anemia, often accompanied by koilonychia.

Faber and his associates[29] studied 10 infants, seven to twenty-four months of age, with iron deficiency anemia, none of whom showed koilonychia or glossitis.

A considerable number of other cases of koilonychia have been reported,[30–45] most of them prior to the widespread recognition of idiopathic hypochromic anemia; in a large number of these cases, it was impossible to find a definite causative factor. Several reports,[2, 30–34] however, suggest strongly that exposure of the hands to chemicals may induce or intensify the condition, whereas other observers[1, 33–36] have noted a family history of koilonychia, and in a few cases,[3, 11, 33–34] koilonychia was apparently present from early childhood.

Summary

A case of idiopathic hypochromic anemia with koilonychia recurring at a seven-year interval in a middle-aged man is reported. On each occasion, both the anemia and spoon nails disappeared completely on treatment with iron.

A survey of the literature reveals that koilonychia is not uncommonly associated with hypochromic anemia of the iron-deficiency type, and that less marked nail changes, such as flattening, increased thinness or brittleness and exaggerated longitudinal ridging, are common enough to be of diagnostic help in the disease.

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MEDICAL PROGRESS

VIRUS PNEUMONIAS. I. PNEUMONIAS ASSOCIATED WITH KNOWN NONBACTERIAL AGENTS: INFLUENZA, PSITTACOSIS AND Q FEVER*

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SINCE the introduction of specific antipneumococcal serums, considerable interest has been centered on the etiologic classification of the pneumonias. Before sulfapyridine came into use, however, bacteriologic procedures were employed primarily for the purpose of determining the presence of a pneumococcus and its type, with a view to possible specific serotherapy and perhaps also as an aid in prognosis. The recent sulfonamide drugs that have been widely used — sulfapyridine, sulfathiazole and sulfadiazine — are more or less equally effective against all types of pneumococci. These drugs vary to some extent in their effect on other bacteria, such as streptococci, staphylococci and Friedländer's bacillus, which may be involved in the causation of pneumonia. The determination of the causative organism thus becomes as important as the pneumoccus typing.

The increased use of bacteriologic diagnostic methods in pneumonia and, particularly, the widespread employment of sulfanilamide derivatives have brought into relief a group of cases in which the common respiratory pathogenic organisms do not seem to play a role and on which the sulfonamides do not have the usual favorable effect. Some of these cases have a number of distinctive clinical features, and are thought to be of virus etiology. Moreover, pneumonias are known to occur in certain diseases of nonbacterial etiology — that is, in diseases caused by known filterable viruses or by rickettsias.

This report deals with the various pneumonias considered to be of nonbacterial etiology, and is divided into two parts. In the first, we present a review of the recent studies dealing with nonbacterial pneumonias associated with known virus or rickettsial agents; these include, chiefly, influenza, psittacosis and Q fever. The second part, which will appear in the next issue of the *Journal*, contains a description of atypical pneumonias of unknown etiology, and a review of the attempts to identify a causative agent in such cases.

INFLUENZA AND PNEUMONIA

The occurrence of serious pulmonary complications in cases of epidemic influenza is well known. Such complications are usually considered to be responsible for the high mortality in certain outbreaks of this disease. Whether the pulmonary lesions are caused by the same agent that gives rise to the influenza itself or are the result of secondary invasions with certain pathogenic bacteria was the subject of considerable controversy during the great pandemics of 1890 and 1918. Most workers considered the influenza bacillus of Pfeiffer to be the significant etiologic agent of both the influenza and its complications during the large epidemic of 1889–1890 and in the smaller outbreaks that followed it.[1] The streptoccocus, however, was thought by some investigators, notably Finkler,[2] to be the cause of the severe and fatal influenzal pneumonias of that period.

Similarly, during the 1918 pandemic, although the influenza bacillus of Pfeiffer was found to be the predominant organism in the lungs in fatal cases of influenza in some regions,[3–7] it was conspicuously infrequent in others.[8, 9] In many localities, the hemolytic streptococcus was apparently the predominant pathogenic organism found during this outbreak, and this organism was particularly frequent in the severe and fatal pneu-

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monias complicating the influenza that occurred in many of the camps of the United States Army.[10–14] During the same pandemic, there were a few reports of outbreaks in widely separated areas of a characteristic type of pneumonia complicating the influenza in which *Staphylococcus aureus* apparently played the predominant role.[15–17] Occasional similar cases have been noted in other small outbreaks.[18–22]

Very similar pathologic lesions were described by a number of different observers during 1918 and were considered, in a general way, to be the characteristic pulmonary lesions of influenza. In some of these cases, the predominant organism recovered from the lungs was the influenza bacillus,[3, 5, 10] in others the hemolytic streptococcus[11, 23] and in still others the pneumococcus.[9, 24] Goodpasture[25] observed typical histologic lesions in the lungs of 2 patients in this epidemic, but was unable to demonstrate any pathogenic bacteria in the lungs, by cultural methods, in histologic sections or after animal inoculations. Interestingly enough, neither of these 2 cases was of the acute fulminating variety: one patient died on the seventh day, and the other died during an exacerbation of symptoms that had apparently persisted for more than six weeks after the onset of the original influenza.

It is now generally accepted that some filterable virus, identical with or closely related to that originally demonstrated by Smith, Andrewes and Laidlaw[26] and later found by Francis,[27] was probably the causative agent in most of the widespread epidemics of typical influenza that have occurred in the last few years. This virus has been labeled "influenza A virus."[28] Viruses immunologically identical with or very closely related to influenza A virus have been shown by direct isolations or by serologic tests to be the causative agent in the extensive epidemic of 1936–1937[20, 21] and also in the one that occurred in 1940–1941.[29–35] In smaller and more localized outbreaks, another virus, now called "influenza B virus," was found to be the cause,[36–39] and there is indirect evidence that possibly a third one and perhaps still others give rise to the characteristic clinical picture in some limited outbreaks.[39, 40]

These findings, however, have not entirely clarified the question of the etiology of the pneumonias that accompany the influenzas during outbreaks. There is some evidence[20, 21] that even cases of simple and apparently uncomplicated influenza may have a spread of the infection to the lungs. The commonest lesion resulting from such an extension, according to Stuart-Harris and his co-workers,[21] who reported on the 1936–1937 epidemic in England, is a diffuse bronchiolitis, which may be distinguished by characteristic physical signs and x-ray shadows. They believe that this represents essentially a true virus lesion because of the relative frequency with which virus was isolated from such cases.

Scadding,[20] in a study made during the same epidemic, distinguished a group of cases of typical influenza with abnormal physical signs in the lungs, with or without radiologic evidence of consolidation. In the less severe cases of this group, only areas of suppressed breath sounds were made out at the lung bases. In some of the severer cases, the clinical picture was that of edematous lung bases without abnormal x-ray findings, whereas in others there were definite areas of consolidation, both clinically and roentgenographically; only the latter cases were associated with a high mortality. The bacteriologic flora of the sputum in this group was very similar to that of cases without influenza, except that pneumococci were apparently more frequent in the cases with consolidation.

Both Stuart-Harris et al.[21] and Scadding[20] described cases of fulminating pneumonia in which the influenza A virus and *Staph. aureus* were isolated from the same lungs at autopsy; the authors believed that the cases were almost certainly due to both these agents. Stokes and Wolman,[22] in 1940, reported a similar case in which both influenza A virus and *Staph. aureus* were isolated from the lungs. In the 1940–1941 epidemic, a number of cases of severe *Staph. aureus* pneumonia complicating clinical influenza were reported from several clinics,[41–43] and the relation of the influenza A virus to some of them was presumptively established.[41, 42] At the Boston City Hospital, *Staph. aureus* was found in almost pure culture or as the predominant organism in all types of cases of influenza, varying from the mild and apparently uncomplicated ones to the fulminating acute and fatal cases with pneumonia, and including a number with a severe and protracted course.[44] Evidence of infection with influenza A virus was obtained in all the various types of cases,[33] either by isolation of the virus or by serologic tests. Interestingly enough, sulfathiazole and sulfadiazine seemed to have a beneficial effect in most of the cases but not in the very fulminating ones. These drugs, however, may have been responsible for the recoveries in some of the very serious cases.

All these findings indicate that under certain circumstances the influenza virus itself may set up a considerable bronchopulmonary reaction, but that in most cases in human beings secondary infection with bacteria plays an important role and

may alter the pathologic picture in the lungs. Analogies are to be found in different animal species.[45–49] In the ferret and in the mouse, for example, the virus alone may produce pulmonary lesions almost identical with those found in fatal cases in human beings, and no pathogenic bacteria can be cultivated from the lungs in these animals.[46–48] In swine, on the other hand, an influenza virus — either the swine strain or a human A strain — gives rise to a mild infection limited to the upper respiratory tract, and pulmonary lesions in this animal result only from the simultaneous infection with the virus and the swine influenza bacillus.[49] In the human disease, it appears that both the virulence of the influenza virus and the prevalence and virulence of the coexisting pathogenic bacteria determine the occurrence and severity of the complicating pneumonias.

Furthermore, pneumonias may appear in patients with influenza during the height of the original attack, or they may have their onset after a varying interval, following apparent recovery from the influenza. In the latter event, it may not be possible to obtain the virus when the patient is first seen during the attack of pneumonia, but serologic tests at that time may reveal a high antibody titer characteristic of patients convalescent from the virus infection.[33, 50, 51] These are evidently relapses of bacterial infection developing in patients recovering from influenza. Typical pneumococcal lobar pneumonia, hemolytic streptococcal or pneumococcal bronchitis or tracheitis and even simple tonsillitis occur under such circumstances.[21] Francis[51] recovered influenza virus on the second day in a patient with pneumococcus Type 3 pneumonia, and Pearson et al.[33] demonstrated high titers or significant rises in titer of influenza A antibodies in many cases of typical pneumococcal lobar pneumonia occurring during the 1940–1941 epidemic in Boston. Such findings indicate that influenza and other severe pulmonary infections may occur simultaneously, or that such infections may follow shortly after an attack of influenza.

Psittacosis, Ornithosis and Related Diseases

A human disease, resembling influenza on the one hand and typhoid fever on the other and associated primarily with atypical pulmonary lesions and acquired from sick parrots, has been known since 1880.[52] Numerous small sporadic outbreaks of such infections, always attributable directly or indirectly to exposure to sick exotic birds, mostly of the psittacine family, were described during the following fifty years. In the years 1929 and 1930, however, there was a pandemic of the disease, having its origin in an epizootic among imported Brazilian parrots but first reported in human cases in Buenos Aires. It was only after this outbreak had spread through many countries all over the world that the disease, psittacosis, gained considerable prominence. It was during this pandemic that the clinical, epidemiologic and pathological aspects of the disease were clearly recognized and its virus etiology was definitely established. A comprehensive review of the early history of the disease and of the outbreak in England is given in the report of Sturdee and Scott,[53] which contains an excellent clinical description of the human disease by Levy-Simpson. This report also contains the classic studies of Bedson and Western, which, together with those of Krumwiede and Armstrong and their associates[54, 55] in this country, established the filterable-virus etiology of the disease. The virus was found to be associated consistently with minute coccobacillary bodies that are now commonly known as "L.C.L. bodies" after Levinthal,[56] Coles[57] and Lillie,[58] the three workers who described them almost simultaneously in Germany, England and the United States, respectively. These bodies are now generally considered to be the elementary bodies of the virus. Enders[59] has recently reviewed the various aspects of the disease and the present status of our knowledge concerning the virus that causes it in a symposium on virus and rickettsial diseases at the Harvard School of Public Health. Meyer,[60] in a recent DeLamar Lecture, presented a comprehensive summary of the biology of the virus and its occurrence in human and avian infections.

There are several reasons for the present intensive interest in psittacosis. First may be mentioned the similarity of this disease to the atypical pneumonias that are now being encountered. In reading the details of the earlier proved cases of psittacosis and the clinical descriptions of that disease that have since been given, one cannot help being impressed with the striking resemblance to the current cases so far as the symptoms, physical signs, roentgenologic and pathological findings and course are concerned. The outstanding differences in the prevalent pneumonias are the failure to obtain a history of exposure to birds, except in certain rare cases that are referred to below; the failure to identify the virus of psittacosis by the usual means[61, 62]; and the lower mortality. In relation to the mortality, one must consider the lower age incidence of the recently reported cases. Most of the deaths from psittacosis have occurred in persons over forty years of age, and the prevalent pneumonias are uncommon in that age group. Furthermore, secondary pneumonias due to bacterial agents have been men-

tioned in cases of psittacosis, but they have not been encountered in the atypical pneumonias now prevalent.[63] This may have accounted for some of the fatalities from psittacosis.

A second reason for the awakened interest in psittacosis is the demonstration of many striking similarities and close antigenic relations between the agent of that disease and a number of other recently discovered viruses.[64–70] Some of these new viruses—those of lymphogranuloma venereum, trachoma and inclusion conjunctivitis—have no constant or apparent relation to acute pulmonary infections. Others were isolated from laboratory animals inoculated with materials obtained from patients with atypical pneumonia or with influenzalike infections. Still others, which were discovered as apparently normal inhabitants of the respiratory tract of certain laboratory animals, are capable of inducing pulmonary lesions in those animals under specified experimental conditions.

Interestingly enough, some of these viruses, such as those of lymphogranuloma venereum, trachoma, inclusion blennorrhea and mouse pneumonitis,[69] are susceptible to chemotherapy with the common sulfonamides, whereas others, including the agents of psittacosis and meningopneumonitis, are apparently not affected.[71] The findings in experimental infections seem to correlate to some extent with published results of sulfonamide therapy in the corresponding clinical conditions. Although sweeping conclusions cannot be drawn from the data thus far available, further investigations of this group of viruses not only may be of theoretical interest but also may uncover new information of value in practical therapy.

Finally, recent studies have indicated a widespread occurrence of psittacosis or psittacosislike viruses in increasing varieties of species of birds all over the world. They have been demonstrated in birds living in the wild state[72–74] and in those bred in aviaries,[60] and have recently been found in pigeons[75–83] and in barnyard fowl.[82, 83] Evidence for latent infections under these conditions has come either from demonstration of the virus in the tissues or by serologic tests in large numbers of birds. These latent infections may, under suitable conditions, become activated and give rise to spontaneous infections or epizootics among birds, or they may give rise to cases in human beings.[79–81] Many of the details of these findings have been summarized by Meyer,[60] who has suggested that the general term "ornithosis" be used to describe the infections in birds or human infections contracted from birds. The designation "psittacosis" would then be reserved for the psittacine infection. The characteristic pulmonary infection might appropriately be called "ornithotic pneumonia" or "pneumonia ornithosa."

A few of the recently uncovered facts about psittacosis that are of immediate interest may be mentioned briefly. Widespread latent infection has been demonstrated among the common varieties of pigeons and doves, even among those found in the parks of New York City.[80, 81] Epizootics have been described in many pigeon lofts, and cases in human beings have been traced to this source. The latent infection in pigeons may be activated by dietary deficiency.[75] Meyer[82, 83] also reported an epizootic among barnyard fowl in New Jersey. This outbreak, which was associated with human infection, may have originated from a sick dove, which roosted among the chickens shortly before they manifested evidences of infection.

It is remotely possible that certain aspects of this problem may have some significance for armed forces based in far-off lands. Such widely scattered countries as Iceland,[74] South Africa[76] and Australia[72, 73, 84] have figured in the recent reports concerning psittacosis. Viruses very similar to that of psittacosis have been isolated from young fulmars, which are birds of the petrel family living on the cliffs off the Faroe Islands and off Iceland, and they were also found in materials obtained from human patients who had acquired their infection while trapping these young birds for eating purposes.[74] In several parts of Australia, epizootics have been described in various species of parrots living in the wild state, and dead birds infected with psittacosis have been found in the bush.[72, 73] Under normal circumstances, the infection of wild birds is usually latent, and is transmitted with difficulty to human beings. From what is already known, however, it is not difficult to imagine situations in which serious human epidemics might arise.

Other Viruses

Other viruses may affect the respiratory tract, although their main clinical manifestations are due to involvement of other systems. In general, the symptoms are those of a grippelike or influenzalike infection. Involvement of the lung to a degree sufficient to give signs by physical or x-ray examinations is rare. The virus of lymphocytic choriomeningitis is an example of such an agent.[85, 86] In experimental animals, vaccine virus may produce a pneumonia whose pathology is similar to that of the atypical bronchopneumonias in man.[87, 88]

Rickettsial Infections

The virus of psittacosis and the related viruses are rather large and pass only the coarser bac-

terial filters. They have many morphologic and other characteristics of rickettsias, but no arthropod vectors have been established. Rashes do not occur regularly in psittacosis. These agents have therefore not been classified as rickettsias, although Lillie[58] had suggested that the psittacosis virus be included among them. They may be said to represent a sort of transitional group between the true filterable viruses and the rickettsias.[66, 67]

Pulmonary lesions, however, have been recognized as part of the clinical and pathological picture of severe rickettsial diseases, notably in typhus and in Rocky Mountain spotted fever.[89, 90] In typhus fever, physical signs of extensive pulmonary consolidation are sometimes made out on routine examination of patients who run the usual course, but the appearance of such signs is usually accompanied by an aggravation of the disease and a fatal outcome.[90] At least in some cases, these pulmonary lesions probably represent infection with the rickettsia and not secondary bacterial infection. Pulmonary complications have recently been reported in cases of South African tick-bite fever,[91, 92] another of the known rickettsial diseases. Experimentally, characteristic lesions have been produced in the lungs of laboratory animals with several varieties of rickettsias, including the different types of typhus, *fièvre boutonneuse* and Rocky Mountain spotted fever.[93, 96]

Q Fever

Like psittacosis, Q fever is of considerable interest at present. The agent of this new disease is quite prevalent in certain parts of Australia and has been isolated and identified in some of the western states in this country. Definite evidence of infection with the agent has been found in this country in certain cases with clinical features closely resemblng those of the current atypical bronchopneumonias. The relevant facts about Q fever and its causative agent are therefore briefly reviewed.

Australian Q Fever

In 1937, Derrick[97] described a new pathologic entity occurring in the state of Queensland, Australia, and gave it the name of "Q fever." Cases, which were first noted early in 1933, increased in frequency in August, 1935. A total of 20 cases had been recognized among 800 employees of one abattoir at the time of the original report, and 9 of the cases were described. Other cases not in meat workers were also noted. Blood and urine from patients, taken during the disease and injected intraperitoneally into guinea pigs, readily established, after an incubation period of eight to fourteen days, an infection having a definite clinical course and pathological findings and giving rise to specific immunity.

The clinical picture in the human cases was quite characteristic. The incubation period was fifteen days or less. The onset was acute, with malaise, anorexia, headache, pains in the back and limbs, and fever. These symptoms increased in intensity until the patient became drowsy and stuporous, as in the so-called "typhoid state." The temperature was usually sustained at 102 to 104°F., but sometimes was swinging in character, especially in those who had taken antipyretic drugs. Fever lasted from seven to twenty-four days, with recrudescences in some cases. The pulse was relatively slow. Chilly sensations were the rule, but frank chills often occurred. One patient had a punctate rash on the fourteenth day, but this was not considered to be characteristic. Jaundice, conjunctivitis, vomiting, abdominal distention and constipation occurred in some cases. There was a slight cough in 2 cases. The spleen was not palpable, and enlarged lymph nodes were not made out. The leukocyte counts were normal, but a relative lymphocytosis was noted in most of the cases after the fever subsided. Slight albuminuria occurred in all cases, and was sometimes associated with granular casts. No mention was made of pulmonary involvement or of x-ray studies.

Improvement in symptoms occurred gradually as the temperature fell — usually by lysis. Convalescence varied with the length and severity of the illness. General and persistent weakness was frequent, and in individual cases, residual anemia, nervousness ("nerves"), corneal ulcer or thinning of the hair was noted.

The agent isolated by Derrick on guinea-pig inoculation was studied in great detail by Burnet and his associates,[98–102] who found it to be pathogenic also for monkeys and mice and possibly for rabbits.[98] Dogs were found to be susceptible but were not considered to play a part in human infection.[103] With mice, these authors were able to obtain primary isolations from human material by the intraperitoneal inoculation of blood.[99, 100] In the spleens of infected mice, they[98] demonstrated typical rickettsia appearing as relatively large intracytoplasmic microcolonies. This rickettsia is fairly large, but is capable of passing a membrane having an average pore diameter of 0.7 micron.[98] Derrick named it *Rickettsia burneti*.[104] It was found to differ from other rickettsias in that it failed to produce agglutinins for Proteus X19 and Proteus XK (Weil-Felix reaction) in animals or in man,[98] and did not give any

cross-immunity reactions with other known rickettsias.[105] Like rickettsias, however, it could be grown in tissue cultures but not in bacteriologic mediums.[101] Suspensions of this organism were prepared from the spleens of mice and utilized as an antigen that gave specific agglutination reactions with immune serums.[99] Specific agglutinins appeared in human cases from the twelfth to the fifteenth day after the onset of symptoms, and were also found in animals after infection.[99]

A series of mild and subclinical infections among the laboratory workers was attributed to the handling of infected animals.[102, 106] These infections were usually demonstrated by the development of agglutinins and protective antibodies,[102] but in some cases there was manifest infection and the rickettsias were demonstrated in the blood.[106]

Epidemiologic studies revealed a widespread prevalence of the rickettsia of Q fever.[107–113] It was found that the bandicoot, a native rodent of the Australian bush, was susceptible to Q fever, and serologic evidence of latent infection was demonstrated in this species.[107] Later, active infection was proved in these animals by the demonstration of the rickettsia in their blood.[109] Evidence of latent infection was obtained in other native bush animals, in certain water rats and other native rats, and also in a cow owned by a person who had previously had Q fever.[111–113]

R. burneti was also obtained from naturally infected ticks collected from bandicoots.[108] It was found possible to infect such ticks experimentally in the larval, nymphal or adult stages by feeding them on infected guinea pigs, and both the latter forms were then capable of transmitting the infection to other guinea pigs.[110] There was also suggestive evidence of transoval passage of the agent in the tick.[110] The feces of the infected ticks were found to be highly infectious and capable of infecting guinea pigs when applied either to the abraded or the intact skin. It was considered likely that human beings became infected through this method of transmission.[110]

Surveys among employees of abattoirs in Brisbane and among foresters working 100 miles from the city showed that the infection was quite prevalent among these workers; the infection, however, was usually latent and demonstrable only serologically. No evidence of infection was found among a group of men in a unit of the militia that had had a short period of training in an area where infected ticks were known to be prevalent. This was interpreted as indicating that these ticks probably do not readily infect human beings.[111] By the middle of 1940, 145 cases, with three deaths, had been studied by the health authorities in Queensland.[113]

American Q Fever

In the spring of 1935, Davis and Cox,[114] working in the laboratory of the United States Public Health Service at Hamilton, Montana, described a filter-passing agent obtained from a group of ticks of the species *Dermacentor andersoni* that were collected in a nearby place called Nine Mile Creek. Later, three more identical strains were recovered from the same species of tick collected in southeastern Wyoming.[115] This agent produced a characteristic febrile infection in guinea pigs, and the agents could then be obtained and transmitted from the blood and urine of the animals. White rats and white mice were also found to be susceptible, but the infection could not be carried beyond the third transfer in rabbits, and monkeys remained afebrile.[114]

This agent, like *R. burneti*, was found to survive in and to be transmitted by nymphal and adult ticks that ingested the agent in the larval stage. It also survived through the eggs deposited by infected females, and was transmitted by the progeny.[116] It was found to be a gram-negative, pleomorphic, rickettsialike organism that occurred both intracellularly and extracellularly in affected tissues of the guinea pig. It grew well in tissue cultures and in the developing chick embryo, but not in cell-free bacterial culture mediums.[117–121]

One of the members of the staff of the National Institute of Health in Washington, D. C., visited the laboratory in Montana for a few days in May, 1938, and during this time handled infected animals and worked with tissue cultures of the new agent. Ten days after he returned to Washington, he contracted an illness resembling Australian Q fever. The onset was insidious, with pain in the eyeballs, a "tired feeling" and a slowly rising temperature that reached a peak of about 103°F. and later dropped gradually. Chilly sensations followed by mild to moderate chills occurred, and later there was a series of drenching sweats for four nights. There were also pains in small joints of two fingers, lasting about three days, at the end of the febrile period. The pulse rate was 90 or lower throughout, and the febrile illness lasted about ten days.[122]

Blood obtained during the height of the fever and inoculated into a guinea pig produced an infection that resulted in the demonstration of an agent identical with the one isolated in Montana.[122] This agent was then shown to be closely related to the rickettsia of Australian Q fever.[105, 123–127] Cox[125] suggested the name *R.*

diaporica to emphasize its filterability. No pulmonary signs or symptoms were mentioned.

The American disease was tentatively called "Nine Mile fever," but Cox[126] later considered the name "American Q fever" preferable. Evidence of the occurrence of this infection was obtained by guinea-pig inoculation, by agglutination tests or by both these methods in persons living in seven different states — namely, Idaho, Montana, Wyoming, Nebraska, Oregon, Nevada and Washington.[126] Bengston[128] has developed a sensitive complement-fixation test that is specific for the common rickettsial infections and should be of great value both for diagnosis and for the demonstration of immunity.

An outbreak of so-called "pneumonitis" ascribed to the agent of Q fever occurred among employees of the National Institute of Health in Washington, D. C.[129] Between March 27 and May 17, 1940, 15 cases occurred among 153 employees of one building, and additional similar mild infections occurred in which x-ray studies either were negative or were not done. One of the patients died. An agent identified as the rickettsia of Q fever was isolated from 3 out of 4 proved cases of pneumonitis, including the fatal case.[130] Specific agglutinins for the Montana strain and for a strain isolated during the epidemic were found in 9 of 12 proved cases and in 1 of 2 suspected cases. No positive tests were obtained in control serums from workers either in the rickettsia unit or in other units, but a few doubtful results were obtained among the former. Specific neutralizing and complement-fixing antibodies also developed in these cases.[128, 130] There was no valid evidence that person-to-person contact or the intervention of an arthropod vector was responsible for the transmission of the disease. Although strains of Q fever had been carried in animals and tissue cultures in one unit of the institute since 1938, the personnel of that unit was spared, and the cases were widely distributed throughout the building.

The clinical features and the physical and x-ray findings in these cases were very similar to those of the various atypical pneumonias currently reported from various parts of the United States. The onset was either coryzalike or with headache, chilly sensations and malaise. There was a latent period of three days after the onset, during which headache was severe and constant, but the patients continued to work. In 1 case, there was a dramatic onset, with abdominal cramps, chills, fever and headache while the patient was at work. Chills, fever, sweats, and pains and aches were frequent. Nausea and vomiting occurred in 3 cases. Several patients developed a hacking cough, which in a few cases was productive of thick, tenacious white mucus, but not "prune juice" or "blood-tinged" sputum. About half the patients had a vague neuralgic type of chest pain that was either substernal or on the side of the lung lesion, but was not pleuritic. All complained of insomnia.

The paucity of physical signs was characteristic. There was no evidence of respiratory embarrassment or any other obvious indication of pneumonia. In some cases, there were areas of dullness or increased breath sounds, or infrequent sticky rales were heard. The pulmonary lesion probably would not have been discovered in most cases except for the x-ray picture. This was the most typical and consistent evidence of the pneumonia. It showed soft, infiltrating lesions, either single or multiple, that were not uniform as in lobar pneumonia but tended to be patchy.[129]

The histopathology in the lungs of the fatal case[131] closely resembled that described by Kneeland and Smetana[63] and by Longcope.[132] Rickettsias were not seen. The spleen showed a picture similar to that found in experimentally infected monkeys[131] and resembled that described in Kneeland and Smetana's[63] case. Lesions in the lungs similar to those found in the human case were also described in experimentally infected guinea pigs[133] and mice.[134, 135]

Two similar cases of American Q fever have been reported from Montana.[136] One patient had typical pneumonitis. Both cases were proved by agglutination tests, and the causative agent was isolated in 1. These infections occurred in the late fall, and both patients had been out in the woods before the onset of symptoms. There was no history of tick bite in these cases, nor was this likely at that time of the year.

Comparative studies of the American strains of *R. diaporica* and the Australian strains of *R. burneti* have been made in both countries and have given fairly uniform results.[105, 122–124] Immunologically, these strains are indistinguishable. Such differences in pathogenicity as have been noted may be ascribed to the lower virulence of the Australian strains, which has been fairly constant according to all the experimental work.

The clinical differences between the Australian and the American disease have already been commented on in the *Journal*.[137] Outstanding is the fact that pulmonary involvement or suggestive symptoms of such involvement have not been mentioned in the Australian cases. This may, of course, be due to the lower virulence of the infecting agent in Australia. It is also possible that such lesions have been recognized more easily in this country because of the readiness with which x-ray films of the lungs are made here, particu-

larly in the classes of patients in whom the reported cases have occurred.

The exact place of Q fever in relation to the etiology of the prevalent atypical pneumonias is not yet clear. Except as already noted, no group of proved cases of pneumonia due to this agent has been reported, although many have searched for it. These rickettsias, like the agents of the psittacosis group, may account for only a small percentage of the cases.

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CASE RECORDS OF THE MASSACHUSETTS GENERAL HOSPITAL

ANTE-MORTEM AND POST-MORTEM RECORDS AS USED IN WEEKLY CLINICOPATHOLOGICAL EXERCISES

FOUNDED BY RICHARD C. CABOT

TRACY B. MALLORY, M.D., *Editor*

CASE 28351

PRESENTATION OF CASE

A fifty-year-old woman was admitted to the hospital because of persistent crampy abdominal pain.

Approximately a week before admission, she became constipated and accordingly took a laxative. After this, she developed generalized crampy abdominal pain, which persisted to the time of admission in spite of repeated enemas. These were productive of small stools and great amounts of flatus. There was no vomiting, and no melena or fresh blood in the stools.

The past history was irrelevant, except that the patient has always been somewhat constipated, requiring the frequent use of mild cathartics. Also, for several years she had had slight, irregular metrorrhagia. Her husband stated that for several years she had complained of mild abdominal aches and pains. She ascribed these pains to the onset of menopause, although she was still menstruating. She had been married for thirty-one years and had had four children.

Physical examination revealed a well-developed and well-nourished woman in no acute distress. Examination of the lungs and heart was negative. The abdomen was markedly distended and tympanitic. Peristalsis was moderately high pitched but not tinkling. Rectal examination was negative.

The blood pressure was 140 systolic, 70 diastolic. The temperature was 99°F., the pulse 80, and the respirations 20.

Examination of the blood revealed a red-cell count of 4,040,000 with a hemoglobin of 12.4 gm., and a white-cell count of 17,400. The blood Hinton reaction was negative. The nonprotein nitrogen was 24 mg. and the protein 6.1 gm. per 100 cc. The urine examination revealed a specific gravity of 1.026 and a ++ test for albumin, and the sediment contained 200 red blood cells and 15 epithelial cells per high-power field.

A flat plate of the abdomen demonstrated that the colon and small bowel were markedly distended with gas. Most of the gas appeared to be within the colon and extended to the region of the sigmoid.

A proctoscopic examination was performed. The proctoscope was passed 18 cm., where on the left anterior wall of the sigmoid, just below the level of the cervix, a localized mass was visualized. Biopsy, performed with difficulty because of pressure from a large heavy cervix, was reported as showing acute and chronic inflammation. A biopsy of the cervix showed chronic endocervicitis. During a barium enema, the barium passed very slowly through the terminal 5 cm. of the sigmoid. The lumen of the bowel was considerably reduced, and frequently went into spasm. No definite filling defects or ulcerations were seen. A second proctoscopic examination was performed. The scope passed 18 cm., but further progress was impossible because of inflexibility of the sigmoid due to an extrinsic mass. A good view of the rectosigmoid was obtained, and no break was found in the mucosa so far as it was exposed. The tumor mass seemed to lie anteriorly and did not involve the cervix.

On the fifth hospital day, an operation was performed.

DIFFERENTIAL DIAGNOSIS

DR. LELAND S. MCKITTRICK: I think perhaps we had better see the x-ray films before starting this discussion.

DR. AUBREY O. HAMPTON: This is the first film, which demonstrates obstruction in the colon. The gas extends down to the sigmoid. The small bowel is more dilated than is usual with a lesion as low as that; it is, nevertheless, only moderately dilated, whereas the colon is markedly so. I am rather surprised that they said this area did not represent a filling defect. I should call it an annular constriction, with a definite filling defect. I do not see the evidence of spasm. That was perhaps observed at fluoroscopy.

DR. MCKITTRICK: This whole picture, to me at least, is difficult to put together logically. The history is short, with a rather sudden onset, and yet the patient came in markedly obstructed, which is unusual, it seems to me, for so short a story. We might try to connect the obstruction in the large bowel with the abdominal aches and pains that she is said to have complained of for several years, but they were quite indefinite, and I do not see how we can put much significance on them.

Metrorrhagia is mentioned, but no vaginal examination is recorded, and I cannot believe the patient did not have an examination.

DR. TRACY B. MALLORY: She had one under anesthesia, and a biopsy of the cervix was done. Evidently the findings were not remarkable.

DR. MCKITTRICK: That is all right. It would be nice to know if she were staining.

There were 200 red blood cells in the urine. How shall I explain that? It seems to me difficult to make all these things fit what I believe is the correct diagnosis.

On the basis of what we know, the patient had something obstructing the sigmoid. She might have had an infiltrating process on the outside that was constricting it, some process within the wall of the bowel itself that narrowed it down, or something within the lumen that caused the obstruction. This woman had had pain for some time, and the abnormal menstrual history makes one wonder if she had an endometriosis that was responsible for the obstruction and menstrual disturbance. I cannot make such a diagnosis with certainty and shall dismiss it. The next possibility is a malignant process in the pelvis, originating in the uterus or ovaries, which had actually extended to the point where it had shut off the bowel. I do not believe it is logical to assume that this occurred.

Then there is regional enteritis or a localized area of ulcerative colitis. These are remote possibilities. A local amebic ulceration, a so-called "amebic granuloma," might be considered, but I do not know how to make such a diagnosis. Diverticulitis should be mentioned, but I do not believe that process would give this picture on proctoscopic examination. Although the x-ray film is often not too accurate at the level of this lesion, it seems quite definite in this case. Sigmoidoscopic examination, too, is sometimes very difficult at this level, particularly if there is fixation of the bowel from something either within or outside the bowel. It would help us greatly in our interpretation if we could be sure — as the examiner stated — that the mass was extrinsic. I do not believe that the pathological report of "chronic inflammation" means anything. We have failed at times to get our specimen from the right place. I must end up by putting my money on the horse that usually wins the race: I must say carcinoma of the rectosigmoid because I do not know what other diagnosis to make. I have not been told anything about the 200 red cells. I do not know what they were doing there, and I shall not make any attempt to explain them.

Dr. Mallory: This patient was operated on because of the severe degree of obstruction. At the first operation, nothing was done but a tube cecostomy, and the bowel was put at rest for nearly two weeks. Then a second operation was done. This time, a fairly thorough exploration revealed a large tumor mass in the region of the rectosigmoid, somewhat adherent to the uterus but movable enough so that it could be resected. It was still considered unwise to attempt a resection at the moment because the bowel contained such large amounts of fluid feces that it seemed risky. On this occasion, a colostomy was done.

Would any of that information lead you to change your mind?

Dr. McKittrick: No, but I suppose you are going to tell me that this was all inflammatory and when the patient came back for operation they did not find anything.

Dr. Mallory: Not so bad as that.

Clinical Diagnosis

Carcinoma of rectosigmoid.

Dr. McKittrick's Diagnosis

Carcinoma of rectosigmoid.

Anatomical Diagnoses

Endometriosis of uterus and sigmoid.
Intestinal obstruction.

Pathological Discussion

Dr. Mallory: At the final operation, the large tumor mass was again found to involve both the sigmoid and the uterus. For that reason, hysterectomy was first performed, followed by an abdominoperineal resection of the sigmoid and rectum. It was necessary to remove a segment of the posterior vaginal wall as well. When we opened the sigmoid, we found that it contained two intramural tumors that projected into the lumen, separated from each other by 2.5 to 3.0 cm. The mucosa over each tumor was perfectly smooth and nowhere ulcerated. The muscularis was markedly thickened, and one could see very clearly the transverse strands of the muscularis running through the tumor — in other words, there was infiltration of the bowel wall without destruction of the musculature. In several places, there were tiny cystic cavities containing blood. On the posterior surface of the uterus were some firm white nodules looking like tumor implants. On section, each of these nodules contained chocolate fluid, confirming the diagnosis of endometriosis. We have seen endometriosis invade and obstruct the sigmoid before, but I do not believe we have ever seen endometriosis so extensive as this in a woman of fifty. She was still menstruating, however.

CASE 28352

Presentation of Case

An eighteen-year-old schoolboy was admitted to the hospital because of a mass in the right thigh.

About three and a half months before entry, the patient was kicked in the thigh while playing football. The resultant slight swelling and stiffness without discoloration lasted only a few days. The injury was then forgotten until a month later,

when the patient noted a firm swelling, somewhat larger than a golf ball, at the site of the former trauma. Following its discovery, this mass grew rapidly. At no time was this lump painful, hot, discolored, numb or throbbing. A month before entry, the patient consulted a physician and was told that he had a "broken blood vessel." There was no loss of weight or fever.

The past and family histories were irrelevant.

On admission, abnormal physical findings were limited to the right lower extremity. In the anteromedial portion of the midthigh was a firm solid rounded mass 10 cm. in diameter. It was not tender, and could be moved by the examiner or by the patient along with the quadriceps muscles.

The pulse, temperature and respirations were normal.

Examination of the blood showed a white-cell count of 7400 and 100 per cent hemoglobin. The blood calcium was 11.3 mg. and the phosphorus 3.8 mg. per 100 cc., and the phosphatase was 4.2 Bodansky units. The blood Hinton reaction was negative. The urine was normal.

A roentgenogram of the right thigh showed a soft-tissue swelling in the anteromedial aspect of the middle third, with linear areas of calcification within the swollen area. This calcification did not run in the direction of the muscle fibers. A roentgenogram of the chest showed a ring shadow in the right apex, probably an artefact. The lung fields were otherwise clear. The heart seemed normal.

On the third hospital day, an operation was performed.

Differential Diagnosis

Dr. Carroll B. Larson: The history leads one to think first of all and most strongly of myositis ossificans. A definite injury, severe enough to result in a hematoma, partially subsided, only to be followed by the appearance of another mass at the same site. This places the lesion on a traumatic basis, and it is well known that trauma initiates osteogenesis, although the mechanism of this process is obscure. The location of the mass is one of the three sites of predilection for the occurrence of osteogenesis following trauma — the other two being in the upper extremity about the deltoid muscle and near the attachment of the triceps muscle. Someone has accounted for aberrant osteogenesis in the abdominal wall on the basis of an embryologic rib remnant, which I am sure does not account for osteogenesis in the thigh. The x-ray films show an area of calcification inside the solid tumor that is globular, well defined and completely separate from the femur. The calcification is generalized, with a sprinkling of more localized calcium deposits, so that it has a dotted-veil appearance that is quite characteristic of myositis ossificans. I do not see that the calcification here follows any definite pattern or direction. An ordinary calcified hematoma gives a different picture and tends to follow fascial planes, for which this mass has no regard, so that I believe we can rule out hematoma.

Malignant tumors must definitely be considered. These might be primary or might originate in a focus of myositis ossificans. In a series of 25 cases of the latter, 1 definitely malignant case was encountered. This is reasonable, when one considers that the elements of normal bone are present in the bone formed in myositis ossificans, which is therefore subject to the changes of any bone, that is, osteogenic sarcoma, fibrosarcoma, parathyroid changes and so forth. It has been a clinical observation that a diagnosis of malignant tumor in myositis ossificans is difficult, and occasionally must be based on the subsequent course rather than on the microscopic appearance.

I doubt whether we can tell from the history, x-ray films or physical examination whether this mass was malignant; the final diagnosis depends on the histologic structure of the tumor and the future clinical course.

Dr. Laurence L. Robbins: Dr. Larson has pointed out the mass and the calcification. I am sure I cannot tell whether this calcification goes with or against the muscle fibers. One thing that is of some importance, at least so far as the history is concerned, is the fact that in the work done at Dillon Field House, Harvard University, the calcification in cases of myositis ossificans usually appeared within three weeks, and increased from that time on. Judging from these observations, there should be a great deal more calcification in this case than there is, if it was myositis ossificans.

Dr. Ernest M. Daland: I should like to say that when we pinned this boy down to a more definite history he said that he had been in a football game but was not certain that this was the point where he had been injured. Certainly, there was no hematoma or ecchymosis.

Dr. Larson: I do not believe that rules out myositis ossificans, because in the largest series that I was able to find only 50 per cent of the patients gave a history of injury.

Dr. Tracy B. Mallory: The chief question in a case of this sort, in which it is obviously impossible to make an accurate preoperative diagnosis, is, What would one do about it?

Dr. Larson: I should like to know one more thing, not recorded in the history: Was there any pulsation or any bruit?

Dr. Mallory: No; there was not.

Dr. Larson: In a case like this, hemangioma is perfectly possible but I do not think it likely;

therefore, the case should be handled with a great deal of caution. Other than that, I do not know a better way of making an accurate diagnosis than by doing it microscopically after biopsy.

When there is a possibility that one is dealing with a highly malignant tumor or with a perfectly benign lesion, one must be certain which it is before the final treatment is decided on.

Clinical Diagnosis

Fibrosarcoma of thigh.

Dr. Larson's Diagnosis

Myositis ossificans.

Anatomical Diagnosis

Synovioma of thigh.

Pathological Discussion

Dr. Daland: I operated with a preoperative diagnosis of fibrosarcoma. Before operation, there was a good deal of discussion concerning the best way to handle this, whether to cut down on it and trust to a frozen section, whether to take a specimen and wait for a final paraffin section, or whether to take the tumor out without exploration. It was decided to take it out and not cut into it. It was our opinion that if it were a fibrosarcoma we should do a great deal of damage by cutting directly into it.

An incision was made over the tumor throughout its entire length and 5 cm. upward and downward beyond it. The skin and fascia were laid back. The fascia was intact and not connected with the tumor. The tumor lay beneath the vastus medius muscle but did not invade it. However, to give a proper margin to the tumor, all the overlying muscle was removed with it. Neither the tumor nor the capsule was cut into. However, when the tumor was removed, there was some rather white fascia in its bed lying along the femur, which suggested the possibility of further tumor. Two sections of this were given to the pathologist for examination. The tumor did not connect with the periosteum or the bone. The femoral artery was left intact posterior to the tumor. The dead space was closed, and the wound closed without drainage. The pathologist was not able to make a definite diagnosis on the gross specimen, but it was not believed that anything different would be done if a frozen-section report were given.

The biopsies of the fascia were reported as negative. In other words, we took out the tumor, all overlying muscle and all the capsule. So often, in operations on fibrosarcoma, there is a temptation to shell it out. I had the experience in one case of shelling out such a tumor and then taking a specimen of the capsule and finding that it showed a fibrosarcoma, which had grown through the capsule. With that case in mind, we determined not to see the capsule at all.

The patient has made a good recovery from operation and has a properly functioning limb. There was a good deal of discussion after operation regarding whether or not, in view of the findings, he should have amputation. I did not advise it. When the time came to consider it, the patient refused amputation.

Dr. Mallory: The tumor was well circumscribed but not encapsulated, fairly firm and pinkish white. There were little foci of calcification, which could be felt with a knife. Grossly, we thought it was a sarcoma. When the microscopic sections came through, we discovered that it was a particular and rather unusual form of tumor. It corresponds with what is described as synovioma, consisting of minute cells as small as lymphocytes but not rounded — either oval or slightly spindle shaped. They have a tendency to be arranged in whorls, so that they produce fibrils or intercellular products. When well differentiated, they often contain elements, suggestive of epithelium, that surround small cystic spaces. These tumors usually occur in the neighborhood of joints, but they are also found in various other places where it is hypothecated that they arise from the synovia of bursas.

The presence of calcification in this tumor interests me considerably. Within a few weeks of receiving the specimen, I saw another case of synovioma, also with extensive calcification. Then Dr. Channing C. Simmons thought back to a case of synovioma that he had had six or seven years ago and got out the x-ray films, which likewise showed calcification. We have considerable calcification in 3 out of 7 cases of these rather rare tumors, so that calcification is a significant diagnostic point; the majority of them, however, do not show it. In another case, which was biopsied in New York City, a diagnosis of myositis ossificans was made. There was prompt recurrence within a few months, and when the patient was operated on here by Dr. George W. Van Gorder, the tumor proved to be a synovioma. The original mass had very extensive bone formation in it. In the other 3 cases that I have cited, there was no bone — just spicules of calcium in the fibrous stroma of the tumor, not in apposition with the tumor cells. In none of these cases was there evidence that the tumor cells directly produced calcification.

The presence of calcium deposits in 4 of the 8 cases of synovioma that I have seen appears to be a point of some significance in differential diagnosis. So far as I am aware, it has not previously been recorded.

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BURNS

Burns, whether thermal, chemical or electric, inflict much damage on the people of this country. When approximately 6000 persons die as a result of such trauma and when countless thousands more are disabled for weeks or months and survive with disfiguring scars, some concerted action by the medical profession should be taken. Many of these burns occur because of carelessness, but some can be classed as "accidental" in the true sense. Both the home and the factory or shop have more than their quotas of persons injured by burns. Much has been done in the development of safety measures and in the emphasis of prevention, particularly by fire departments and insurance companies. So far as therapy is concerned, great strides have been made in the last ten or fifteen years. Numerous investigators have made careful studies of groups of cases and have presented their findings. As a consequence of these studies, lives have been saved, and the functional and cosmetic results have been infinitely better.

Within the next year or two, chemical burns from war gases may add to the toll already being exacted by other chemicals, heat and electricity. Instructions have been formulated for the management of burns due to these agents and have already been distributed by the proper authorities.

Every physician is liable to be called at some time in his life to handle a severe burn. Not only should adequate provision be made in medical schools for instruction in the modern management of such cases, but the results of newer methods should, perhaps, be made known to physicians in active practice. An authoritative summary of accepted therapeutic measures, such as that presented in this issue of the *Journal*, should do much to bring to the attention of the physician the methods that will prevent fatalities and lessen disability. This information deserves careful consideration.

PAN-AMERICAN MEDICINE

The war is bringing about a greater exchange of medical ideas between the continents of North America and South America. The Pan-American Medical Association has attempted to foster, and desultory visits of physicians have tended to promote, a better understanding between the two continents for a number of years. More recently, the plan of training young medical men from South America and Central America as medical fellows under the guidance of General Hugh S. Cumming of the Pan-American Sanitary Bureau has brought numerous young physicians to this country. At the meeting of the American Medical Association in Atlantic City, there was increased evidence of co-operation between the two continents: the Scientific Exhibit contained striking examples of investigations made in countries

outside the United States, and the participation of South American and Central American physicians in the proceedings contributed greatly to the international character of the meeting. In addition, the presence in the *Journal of the American Medical Association* of a larger number of abstracts of papers appearing in the medical periodicals of these other countries indicates a growing appreciation of medical matters of mutual interest, and a sanitary-engineering survey of South America now under way will undoubtedly lead to further co-operation. Such an interchange of medical thought will undoubtedly contribute much to medical advance.

MEDICAL EPONYM

Raynaud's Disease

A. G. Maurice Raynaud (1834–1881) described this disease in a thesis submitted to the Faculty of Medicine in 1862 and entitled *De l'asphyxie locale et de la gangrène symétrique des extrémités* [*Local Asphyxia and Symmetrical Gangrene of the Extremities*] (Paris, 1862: 174 pp.). A portion of the translation follows:

> I propose to demonstrate the existence of a kind of dry gangrene affecting the extremities, which it is impossible to explain by vascular obliteration; a kind that is characterized particularly by a remarkable tendency to symmetry, in that it always affects similar parts, the two upper or lower extremities, or all four at once; furthermore, in some cases, the nose and the ears are affected, and I shall endeavor to prove that this species of gangrene is caused by a disorder in the innervation of the capillaries. . . .

R. W. B.

MASSACHUSETTS MEDICAL SOCIETY

COMMITTEE ON MATERNAL WELFARE

Case Report: Operative delivery followed by shock and death

A thirty-six-year-old para III was sent to the hospital. The past history was entirely irrelevant. The two previous pregnancies had terminated normally with living children. The labor of the third pregnancy was long, and after two hours of strong second-stage pains, forceps delivery was attempted at home but was unsuccessful. On admission, the patient was given ether, and a difficult midforceps extraction was accomplished. A living child was obtained. Immediately after delivery, the pulse became very rapid, although there was no unusual bleeding. The patient was not transfused, but intravenous glucose and stimulants were administered. Death occurred one hour after delivery. An autopsy was not performed, and the death certificate was signed "organic heart disease and cardiac decompensation."

Comment: Since there is nothing in the past history of this patient to suggest organic heart disease and cardiac decompensation, and since no autopsy was performed to confirm this diagnosis, it seems much more probable that death was caused by post-partum shock. In all probability, this fatality was due solely to poor obstetrics. The delivery in the hospital was described as "difficult"; nevertheless, it was successful, and a living child was obtained. It is fair to conclude that had this patient been hospitalized at the beginning of labor, the same operation would not have been difficult several hours earlier, and that shock and death would not have resulted.

DEATH

HOGAN — Daniel J. Hogan, M.D., of Roslindale, died August 15. He was in his fifty-sixth year.

Dr. Hogan received his degree from Tufts College Medical School in 1920. He was a major in the United States Army Medical Corps, and a member of the Massachusetts Medical Society and the American Medical Association.

His widow survives him.

WAR ACTIVITIES

CIVILIAN DEFENSE

Instructional Films

An excellent sound film, "Emergency Medical Service," is now available for medical units. It shows how an emergency medical service operates in co-operation with the other civilian-defense services, and the accompanying sound disk explains clearly the operations of the unit. The showing time is twenty-one minutes.

This film and other very good instructional 16-mm. sound and silent films on first aid, chemical warfare and first aid for gas casualties are available through the Film Department, Speakers' Bureau, Massachusetts Committee on Public Safety, 18 Tremont Street, Boston. These films are loaned to any medical unit that specifies the date on which the films are desired, guarantees the cost of shipment and provides suitable equipment and the services of a competent operator.

MISCELLANY

RÉSUMÉ OF COMMUNICABLE DISEASES IN MASSACHUSETTS FOR JULY, 1942

Diseases	July 1942	July 1941	Five-Year Average
Anterior poliomyelitis	8	5	9
Chicken pox	436	519	421
Diphtheria	22	9	13
Dog bite	1276	1286	1228
Dysentery, bacillary	0	24	30
German measles	211	116	56

Gonorrhea	413	344	386
Measles	1157	1420	1359
Meningitis, meningococcal	14	5	3
Meningitis, other forms	7	8	—
Mumps	555	533	330
Paratyphoid infections	9	4	11
Pneumonia, lobar	100	155	163
Scarlet fever	335	232	235
Syphilis	427	388	425
Tuberculosis, pulmonary	346	204	286
Tuberculosis, other forms	23	28	28
Typhoid fever	4	4	7
Undulant fever	4	4	4
Whooping cough	884	659	558

Geographical Distribution of Certain Diseases

July, 1942

Anterior poliomyelitis was reported from: Boston, 1; Newton, 1; Orange, 1; Palmer, 1; Somerville, 2; Warwick, 2; total, 8.

Diphtheria was reported from: Boston, 2; Brimfield, 1; Fall River, 16; Norwood, 1; Warren, 1; Woburn, 1; total, 22.

Meningitis, meningococcal, was reported from: Boston, 1; Cambridge, 1; Chelsea, 1; Fall River, 1; North Brookfield, 2; Northampton, 1; Somerville, 2; Westover Field, 1; Worcester, 4; total, 14.

Meningitis, other forms, was reported from: Boston, 2; Brockton, 1; Chicopee, 1; Framingham, 1; Pittsfield, 2; total, 7.

Paratyphoid infections were reported from: Barnstable, 1; Beverly, 1; Lawrence, 2; Ludlow, 1; Melrose, 1; Norton, 1; Somerville, 1; Watertown, 1; total, 9.

Septic sore throat was reported from: Arlington, 1; Athol, 1; Boston, 5; Holliston, 1; Newton, 1; Waltham, 1; Winchendon, 1; total, 11.

Tetanus was reported from: Boston, 1; total, 1.

Trichinosis was reported from: Winchendon, 1; total, 1.

Typhoid fever was reported from: Dunstable, 1; Natick, 1; Watertown, 1; Worcester, 1; total, 4.

Undulant fever was reported from: Bridgewater, 1; East Longmeadow, 1; Franklin, 1; Southbridge, 1; total, 4.

Communicable diseases reported at figures below their five-year averages were anterior poliomyelitis, bacillary dysentery, measles, paratyphoid infections, lobar pneumonia, tuberculosis (other forms) and typhoid fever.

Diseases reported at figures above their respective five-year averages were chicken pox, diphtheria, dog bite, German measles, gonorrhea, meningococcal meningitis, scarlet fever, syphilis, tuberculosis (pulmonary) and whooping cough.

Mumps reached record-high figures for the eleventh time during the past twelve months.

One case of animal rabies was reported from Whitman, maintaining the newly discovered focus in the southeastern section of the State.

CORRESPONDENCE

WILLIAM H. WELCH

To the Editor: In your interesting editorial remarks in the July 23 issue of the *Journal*, regarding the life of William H. Welch, by the Flexners, there is one statement which I think is incorrect. You speak of Dr. Welch's great-grandfather as having been a physician. You will recall that his grandfather was married twice. His first wife was the daughter of a physician, and three of her sons became physicians. However, William H. Welch's father, William W. Welch, was not one of these three but was the son of Dr. Benjamin Welch's second wife and she was not the daughter of a physician. It would appear that Dr. William H. Welch just escaped having a great-grandfather who was a physician.

C. J. Bartlett, M.D.

New Haven, Connecticut

* * *

Dr. Bartlett is correct. Dr. Welch's great-grandfather was *not* a physician; the Flexners' book was misquoted. Ed.

'WORLD CONFLICT AND MEDICAL SERVICE"

To the Editor: This letter was called forth after reading Mr. John M. Pratt's article in the July 30 issue of the *Journal*, entitled "World Conflict and Medical Service."

In summary, the article seeks support for the National Physicians Committee for the Extension of Medical Care, whose program is educating the American people through press and radio to resist "political tinkering in the field of medicine." By so doing, it feels it has made its utmost contribution to the war effort.

This letter is written in the firm conviction that the program as advocated by the article is neither a significant nor a basic addition to America's fighting capacity.

This is a time of grave crisis for the world and our country. The job of the American medical profession is to provide medical care to the whole of a busy population which is dedicating every energy to victory over the Axis. The Army needs 45,000 doctors by January 1, 1943. This means operating on two thirds of our peacetime personnel for civilian needs.

To complicate matters still further, there has been a dislocation of large segments of population necessitated by the growth of mushroom communities in defense areas. This has not been followed by a corresponding shift in the medical profession. The times demand a closer guard on the health of our industrial population than ever before. How are we to meet this new problem of dealing with an expanded assignment with a drastic reduction in personnel?

The populace of these neglected defense communities may well wonder where the solution to their problems lies. The government, through its various agencies, is concerned over this shortage of physicians and their reallocation. People are looking to their government as well as to the medical profession for relief of this neglect. Herein lies the threat of "political tinkering in the field of medicine" which Mr. Pratt is laboring to avoid.

What is Mr. Pratt's program for alleviating these conditions? If a mother in one of these defense communities cannot get a doctor for her ailing child, Mr. Pratt would write editorials keeping her "conscious of the general superiority of American medicine." He would teach her "what she has to gain or lose by substituting a political control of medical care for our system of independent medicine."

This is a new problem and it demands a new answer. No program whose only point is to encourage categorical rejection of government help is worthy of support in these times. It is a disservice to America's war effort to imply that the government cannot be expected to handle itself capably with regard to medical care for Americans. Especially is this so, when the National Physicians Committee for the *Extension* of Medical Care (italics ours) makes no more constructive suggestions than it does.

What is needed is an immediate co-ordinated offensive against this problem of wartime medical care, bringing

together the interested government agencies, such as the United States Public Health Service, Federal Security Agency, Woman's Bureau and Children's Bureau, with the organized medical profession. What is needed is better distributed medical care, more efficiently used. The immensity of the task can countenance no refusal of help, and can afford no such half-hearted attempts as that made by the program suggested in the article referred to.

MARJORIE HAYES, M.D.
LESLIE EPSTEIN, M.D.
ASHER GORDON, M.D.

Johns Hopkins Hospital
Baltimore, Maryland

REPORTS OF MEETINGS

SUFFOLK DISTRICT MEDICAL SOCIETY

The regular spring meeting of the Suffolk District Medical Society was held at the Boston Medical Library on April 29, with Dr. Albert A. Hornor presiding. The paper of the evening, "Virus Infections of the Nervous System," was delivered by Drs. H. Houston Merritt and Luther Thomas, of the Boston City Hospital.

Dr. Merritt discussed the clinical aspects of the problem, with special reference to some of the commoner diseases encountered in which a virus may or may not have an etiologic role. Of conditions affecting the peripheral neurones, infectious polyneuritis is the only one considered possibly of virus origin. There is usually, but not always, a subacute onset, with a gastrointestinal or respiratory upset. This is followed in seven to ten days by facial diplegia and quadriplegia, with hyporeflexia but no diminution of sensation. The cerebrospinal-fluid protein is invariably elevated to 100 to 500 mg. per 100 cc. Although infectious polyneuritis was formerly considered a benign condition, a mortality as high as 25 to 40 per cent has been reported in some series. Even though no virus has been isolated, the presence of a peripheral reaction of virus pattern without central involvement is considered suggestive evidence of such an etiology.

Of diseases of the spinal cord, herpes zoster may be due to a virus, whereas anterior poliomyelitis most certainly is. The former involves primarily the posterior-root ganglions, but the associated inflammatory changes in the posterior and even the anterior horn are very similar, in fatal cases, to the findings in poliomyelitis. The supposedly responsible virus has never been isolated from any tissue. In anterior poliomyelitis, on the other hand, a virus can be obtained, not only from the central nervous system, but even from the cerebrospinal fluid, if proper technic is employed. The primary pathologic change is destruction of the anterior-horn cells, and any inflammatory changes are undoubtedly secondary. Changes also occur in the posterior horn, the white matter and cerebrum, but any central-nervous-system reaction is also probably secondary.

The outstanding virus infection of the meninges is lymphocytic choriomeningitis. This interesting and thoroughly benign condition may occur at any time of year in any person of any age or sex. Its natural course is two or three weeks, but spinal-fluid changes may persist longer. The infection embraces a wide group of cases with similar clinical and laboratory pictures but probably of various and questionable etiology. There may be an acute or subacute onset of characteristic meningitis, with an increase of cells in the cerebrospinal fluid to 500 to 1000 per cubic millimeter, all lymphocytes. The sugar content is normal, in contrast to the findings in tuberculous meningitis. In the initial stage, systemic manifestations occur, with gastrointestinal or respiratory upsets of three or four days' duration. Following a latent period of three to seven days, involvement of the central nervous system, with findings characteristic of meningitis, takes place. After running its natural course of two or three weeks, there may rarely be a complicating myelitis.

The number of conditions of the encephalon in which a virus is suspected of an etiologic role is steadily increasing. These are mostly epidemic, with a few sporadic cases in the interim. Although few of these at present create a serious clinical problem, their nature is such that there may be serious outbreaks under present conditions, when men and horses are being rapidly moved in large numbers. Eastern equine encephalitis is the best known in this region, but there is also a Western type. A virus was suspected in the Eastern variety in 1932 but was not confirmed until 1938. The mortality is about 60 per cent. Children seem most susceptible to this disease, which occurs largely in the summer. The onset is abrupt, with the initial dramatic central-nervous-system manifestations of stupor, convulsions and localizing signs and without any prodromes. The cerebrospinal-fluid pressure is elevated, and there are 1500 to 2500 cells per cubic millimeter, of which 60 to 80 per cent are polymorphonuclear neutrophils. The sugar content is normal, in contrast to that in acute bacterial meningitis. The disease may early be confused with brain abscess. Patients who recover are often left with some residuum, such as paralysis or loss of speech. Pathologically, there is intense perivascular infiltration. In the Western type, the mortality is variable but lower (7 to 40 per cent), and adults are more frequently attacked. Focal signs are less common, coma and tremors being the usual manifestations. Also, the inflammatory changes in the cerebrospinal fluid and in autopsy material from the brain are not so intense. St. Louis encephalitis was recognized in 1933 during an epidemic of 1000 cases, which occurred in both adults and children. The mortality is about 20 per cent. The onset is usually in the central nervous system, with headache, stiff neck and tremors. Some cases are very mild, and would be unrecognized except for the presence of an epidemic and the finding of immune bodies. Some later epidemics have been combinations of this virus with the Western equine variety. Another group of encephalitides includes the Japanese, Australian and Russian types. The manifestations of these are alike and similar to those of the St. Louis variety. As in most of these, differentiation depends largely or wholly on immune reactions. Von Economo's encephalitis lethargica, which some contend is not caused by a virus, was first recognized in an epidemic in 1918 and was sporadic until 1923. Symptoms are variable, but eye-muscle disturbances are common. Any part of the central nervous system may be involved, and the mortality is about 50 per cent. Residual processes are frequent and important, especially parkinsonism. The histology is almost identical with that of anterior poliomyelitis except that the intensity of the lesions in the brain and spinal cord is reversed, which is one of the reasons for considering this a virus disease.

Among diseases more questionably of virus etiology are postvaccinial encephalitis and acute encephalomyelitis. Encephalitis may also follow rabies, measles and influenza. Eight to fifteen days following one of these diseases, there may be nervous-system manifestations. Except for a slight leukocytosis in the cerebrospinal fluid, there are no significant changes. Although this syndrome is usually present after virus infections, it may occur after acute bacterial

infections. Therefore, it is probably allergic rather than viral in origin. In acute encephalomyelitis, the onset is abrupt, and the involvement widespread. The patients either succumb or recover only to have some residuum. In the latter event, the disease is often diagnosed as multiple sclerosis. But the onset of the latter disease is usually less widespread, and one group of symptoms and signs disappears as others occur. There seems no evidence of a virus etiology for this syndrome.

In conclusion, Dr. Merritt pointed out that, from 1928 to 1938 at the Boston City Hospital, 1 in 3680 admissions and 1 in 126 neurologic admissions were for encephalitis.

Dr. Thomas then discussed some of the investigative problems. The equine and St. Louis encephalitides, although caused by different viruses, may merge during epidemics. At present, there is no way of determining whether these diseases will continue to increase in incidence or disappear, as the Australian X disease did. But whereas equine encephalitis was originally considered solely animal, it and louping ill have become human and may be forerunners of other animal diseases now studied in the laboratory. The classification of virus diseases of the nervous system cannot be based on histologic findings because of their lack of specificity and consistency. Attempts have been made to class them as epidemic and nonepidemic, neurotropic and pantropic, and according to whether their virus etiology is proved, probable or suspected.

Laboratory detection of a virus is difficult, and identification is usually dependent on immune reactions. This may be carried out by injection of the unknown material into animals vaccinated against known viruses, by neutralization of the injected material with various antiserums before injection and by some newer in vitro methods.

Dr. Thomas then considered the epidemiology and immunology of specific diseases. St. Louis encephalitis has been increasing geographically since the first epidemic in 1933, and is often associated with Western equine encephalitis. The virus can be isolated only from the central nervous system in fatal cases, but immunization may be carried out by nasal irrigation in known cases or infected animals. These late summer epidemics are mosquito borne and have their perpetuation in stagnant water. Horses have shown evidence of previous attacks in immune reactions. Antibodies appear in two weeks and persist indefinitely. The virus must be identified in the blood and cerebrospinal fluid for its etiologic role to be proved.

Western equine encephalitis has been increasing in man each summer since 1937. This virus has been isolated from the blood and cerebrospinal fluid in active cases, as well as from post-mortem material. Its presence in ticks, as well as in many animals, birds and mosquitoes, may explain some dry-season epidemics. Neutralizing antibodies are found early, whereas complement-fixing ones may persist for three years.

Eastern equine encephalitis, known in horses since 1933 and in man since 1938, is immunologically distinct from the Western variety but is transmitted similarly. Its virus has been isolated only from autopsied central-nervous-system tissue. Neutralizing antibodies have been demonstrated as early as six to eight days.

Other forms of encephalitis are of less practical importance. Australian X disease may be the same or similar to louping ill, but its virus has been lost and the disease seems extinct. Japanese B encephalitis is apparently very similar to the St. Louis type in manifestations and epidemiology. Russian forest-spring fever is carried by a rodent-tick combination. Louping ill, transmitted by a sheep tick, has caused rare cases in laboratory workers. The B virus of the monkey may be responsible for a rare case of fatal ascending myelitis. Lymphocytic choriomeningitis occurs naturally in mice, in which the manifestations, however, are nonspecific. It can be transferred in utero. Transmission to human beings can often be traced to recent handling of mice, and even home rodents are not above suspicion as carriers. The virus apparently may enter the intact skin. Insect transmission is possible but of no practical significance as yet.

Von Economo's disease has always been clinically suspected of having a virus etiology, but none of the present known strains have been identified. Similarly, infectious polyneuritis and herpes zoster are considered to be viral in nature, but the responsible agent still escapes detection.

Dr. Henry R. Viets opened the discussion by pointing out that there may be multiple invasions by viruses. Strong antibody titers may be observed for as long as seven years. Dr. Conrad Wesselhoeft stated that one virus activating another may be the mechanism behind certain postinfectious encephalitides. Of 4 patients who developed encephalitis during the third week of measles, 3 were found to have the virus of the Eastern equine strain. Post-measles encephalitis is not uncommon, but there are surprisingly few personality changes in relation to the amount of coma accompanying the attack. In mumps, encephalitis may be concurrent or even initiating, as well as occurring during convalescence. In the former event, it is often difficult to rule out the diagnosis of preparalytic poliomyelitis. As many as 800 leukocytes per cubic millimeter may be found even in routine spinal fluids from patients with mumps, which leads to the suggestion that this is really a systemic disease.

BOSTON CITY HOSPITAL

The first of a series of lectures sponsored by the Boston City Hospital House Officers' Association as a preparation for physicians entering the armed forces was given on May 5 at the hospital.

Dr. Donald W. MacCollum spoke on "The Practical Management of Burns." He first considered thermal burns. First-aid instruction for the layman should emphasize the care of shock in any burn. If a physician is not present but available, the burned area should be covered with clean linen. In minor burns, the patient may be taken to a first-aid post, but in the more extensive cases the doctor should be brought to the patient. Tannic acid ointment should not be applied to any burn at this stage. If a physician is not available for several hours, minor burns should be washed under running water, if that is available, and should otherwise be covered with a paste of sodium bicarbonate and water. The area is then loosely wrapped with an abundant clean bandage, and the patient is sent to a doctor. For extensive areas, easily removed clothing is gently removed without further attempts at cleansing; the patient is covered with clean clothes soaked in a warm solution of sodium bicarbonate, kept warm, given tea or coffee by mouth and hurried to a hospital. The important points to be remembered are: tannic acid jelly or strong tea should not be applied to a burn before it has been properly cleaned; grease in any form should be avoided; the patient should not be manipulated unnecessarily in an attempt to apply a neat bandage.

First-aid instructions to physicians emphasize the value of examining and treating the patient for actual or in-

cipient shock before the burn is cared for. For this purpose, the control of pain with adequate amounts of morphine is very necessary, and the dose should be double that usually administered before an elective operation on a patient in shock. In severe shock, oxygen by some method, intramuscular caffeine and plasma, if available, should be given. The last is administered intravenously at the rate of 5 cc. per pound of body weight. In its absence, physiologic saline solution, 10 cc. per pound, may be temporarily given. Only after shock has been combated should the burn be evaluated. If the burn is minor, cleansing is carried out by gentle washing for seven minutes with sponges soaked in 50 per cent solution of green soap (not tincture) and 50 per cent hydrogen peroxide. Débridement is done only with sterile instruments, and the area is then flushed with copious amounts of physiologic saline solution or distilled water, dabbed dry, and dusted with one of the sulfonamide powders. Burns of the hands, feet, face and genitalia are covered with a sterile ointment and bandaged as well as possible. Elsewhere, tannic acid jelly or triple dye may be employed. Splinting should be carried out wherever indicated for the best orthopedic results. In the event of a major burn, only the adherent clothing and the gross contamination, without extensive cleansing, are removed. One of the sulfonamide powders or an emulsion or suspension in a water-soluble base is then liberally applied. If powders are used, they should be covered preferably with a water-soluble jelly, since they are more easily removed than the sterile ointments and triple-dye jelly, which, however, may be used. Thick bandages, to prevent soaking through and further contamination, are applied, with a surrounding pressure bandage if possible, and the victim is hurried to a hospital. The major points in this group are: the shock should be treated before all else; tannic acid ointment should be applied only after the area has been cleansed, and never to the hands, face, feet and genitalia; adequate doses of morphine should be used; the sulfonamide powders should not be allowed to enter the nose and eyes, where they are very irritating; and a very thick bandage should always be applied over extensively burned areas.

Hospital treatment of burns of minor degree is essentially that described above under first-aid treatment by physicians. In major burns, the degree of shock should be checked clinically, and further treatment in the form of heat, morphine and so forth should be administered. If time permits and facilities are available, determinations of the red-cell count, hemoglobin, hematocrit and serum protein are helpful but not necessary. Additional plasma in the amounts recommended above should be given. Whole blood should not be used except when there has been blood loss from other injuries. Anesthesia is employed if indicated, the intravenous or rectal route being chosen if there is any question of hot air or gas inhalation. The area is cleaned and débrided as described above, under sterile precautions. Burns of the hands, feet, face and genitalia are dusted with one of the sulfonamide powders, covered with a sterile ointment and bound with thick layers of gauze, and the extremities are splinted. For burns elsewhere, a similar routine may be carried out only if one is prepared to combat the fluid loss with repeated plasma transfusions. Usually, it is better to employ one of the escharotics to prevent serum loss, but specialized aftercare is probably one of the more essential features of this type of burn. This includes a clean, electrically heated bed, frequent evaluation of the blood chemistry, adequate oral and parenteral fluid intake, and constant medical and nursing care.

The hospital treatment of old burns differs in certain respects from that outlined above. The use of the sulfonamides in the first-aid treatment increases the period during which débridement may be carried out to as long as thirty hours after the burn has been received. Otherwise, this procedure is contraindicated later than eight hours, since the area should be considered already infected. Shock treatment is still the first consideration. The patient is then immersed in a tub of warm tap water, with constant exchange of water for several hours. After gentle drying, the sulfonamide powder of choice is used and is followed by a sterile ointment. Tannic acid in any form is contraindicated. If the burn is crusted, the area may be first covered with what some consider the dressing of choice in old burns, namely, wet saline or *tulle gras* with Eusol — a chlorinate compound made of slaked lime and sodium bicarbonate.

Grafting should not be necessary in second-degree burns, and in deeper ones the kind and amount of graft depend on the extent and site of the burn. Special preoperative precautions are taken to have the patient in the best possible condition generally and locally. The important conditions for successful results are to have the granulations cleaned at least to their fibrous base, which in cases of contractures should be removed. Island or Reverdin grafts should be strictly avoided for the best cosmetic results and for the shortest convalescence.

The second large group of burns are those caused by chemicals. The first warning here is for the attendant to protect himself. Mustard gas is really a fine oily vapor, and the exposed areas must be attacked early. All clothes are removed and decontaminated. Then, the victim is given a thorough soap-and-water scrub, followed by shaving of hairy regions if they have been affected, for they are not otherwise easily cleaned and may develop subsequent burns. If this is done in less than a few hours, there is no need for further treatment, but the patient should be observed temporarily. In patients seen after eight hours, the burned areas are treated like any old burn. One should always consider the possibility of damage to the pulmonary structures if anesthesia is contemplated, and morphine for shock should be avoided for this same reason.

Treatment of exposure to lewisite liquid is of no value after one minute. Within that time, the area should be bared of all covering, and the wound repeatedly swabbed with hydrogen peroxide, which is continued for half an hour. The area is then washed for seven minutes with soap and water, and an alcohol pad is applied and left in place for five minutes. A dry dressing is applied, and if no blister appears in twelve hours, the patient may be discharged. If blisters develop, they are then treated carefully, so that none of the fluid escapes onto the surrounding skin, for it contains the same arsenical as the original fluid and will cause grave injury. Even a small amount of this material will be fatal if it reaches the blood stream through any route. If blisters have broken and the patient shows signs of arsenical poisoning, the entire area is widely excised, and immediate graft carried out. Sodium thiosulfate is the drug of choice in combating systemic poisoning.

Phosphorus has the peculiar property of continuing to burn even after being imbedded in the flesh. If there is none still active, the area may be treated as a thermal burn. But if bits of the material are smouldering on or in the skin, the region must be kept wet, preferably with warm water. Five to 15 per cent copper sulfate may be applied if available, for it will temporarily stop the burn-

ing. But the phosphorus particles must be removed by some method before the patient can be considered out of danger. Thereafter, the treatment is the same as that for any burn.

Acids and alkalies, contrary to popular belief, should not be neutralized, for in that way the heat generated or the neutralizing agent may cause a burn. It is preferable to use continuous running water or to immerse the victim in a tank or nearby body of water. The only exception to this is that excess lime is wiped off before wetting.

Electrical burns are deceptive from the first. One should not be overzealous in attempting to remove a patient from the scene before first determining that the current has been disconnected or that the rescuer is properly insulated. The patient should not be regarded as dead until rigor mortis sets in, for several cases are reported of recoveries after many hours without a perceptible heart beat. Almost all these burns are third degree or more because of the intense heat and coagulation of the blood in the vessels supplying the area. Coagulation may cause slough on the seventh to tenth days, sometimes with hemorrhage. The area is treated like any burn except that no eschars are applied, and daily dressings are done to follow the progress of the slough if there is any. Sloughed areas are not surgically removed but are allowed to separate, for the amount of tissue thus lost is much less than would have been computed at an earlier stage. Sterile hemostats and a tourniquet should always be at the bedside, to guard against the danger of hemorrhage at the time of separation of the slough.

BOOK REVIEWS

Allergy in Clinical Practice. By staff members of the Cleveland Clinic. Under the direction of Russell L. Haden, M.D., chief of the Medical Division. Edited by J. Warrick Thomas, M.D., chief of the Section on Allergy. 8°, cloth, 370 pp., with 92 illustrations, including 14 in color. Philadelphia: J. B. Lippincott Company, 1941. $5.00.

This book is an endeavor to present the various phases of allergy as applied to general practice. The well-known manifestations of allergy with reference to the upper and lower respiratory systems and skin receive major emphasis, with some consideration of the less common reactions on the gastrointestinal, ocular and endocrine systems. The presentation is orderly and marked by clarity and brevity. In fact, if what appears to be a disproportionately large number of illustrative case reports were considerably reduced, one would be left with a concise monograph summarizing the general principles of allergy without appreciable loss of practical value.

The Advancing Front of Medicine. By George W. Gray, A.B. 8°, cloth, 425 pp. New York: Whittlesey House, 1941. $3.00.

It is a task of no little difficulty to present matters of scientific research to the public so that they are readily understandable, to convey the facts with accuracy and the significance of those facts with clarity. But Mr. Gray has achieved it here with almost astonishing perfection. He has done it, moreover, without resorting to the false sensationalism that so often offends in similar pieces of reporting. And the more, because he is an outsider looking in, does one marvel at his restraint and judgment.

But Mr. Gray's "front" should really be fronts. He has chapters on the nature of disease, on heredity, on the vitamins (on which the public has been so perniciously exploited), on the blood and its disorders, on hypertension, on the sulfonamide drugs, on influenza, on allergy, on the relation of anxiety to health, on epilepsy and certain other nervous disorders, on sleep, on pain and its relief, on drinking, smoking and drug addiction, on cancer and on growing old.

With its wide range, its sane way of weighing and balancing and its bits of history, this book is revealing even to a physician; how much more so, then, to the layman, to whom nearly all its matters must come as something fresh and new. Perhaps its selection by the Scientific Book Club will increase its circulation; it deserves a wide one, for it is capable of doing a great deal of good.

Diseases of Women. By Harry S. Crossen, M.D., and Robert J. Crossen, M.D. Ninth edition, entirely revised and reset. 4°, cloth, 962 pp., with 1127 engravings, including 45 in color. St. Louis: The C. V. Mosby Company, 1941. $12.50.

This is the ninth edition of a very familiar textbook on diseases of women. The greatest advances that it heralds are those of endocrinology and chemotherapy. The former has imposed on the whole field of gynecology a physiologic approach in place of the anatomic and pathologic. As a result, one gets a picture of a changing and cyclic rather than a static group of organs. The adaptation of the newer hormonology to clinical use has been well treated by the authors. There is a scarcity of information about stilbestrol, which might well be explained by the rather recent release of this drug by the Council of Pharmacy and Chemistry of the American Medical Association.

This is not an operative book, but rather a treatise on diagnosis and therapy. Preparation for operation and postoperative care are discussed, but the technic of surgical steps is not included. Because of the scope of this work, one hesitates to single out any particular portion for special comment. However, the sections on pessaries, endometrial biopsy and the Rubin test are examples of the fine detail that makes this study so valuable to the practitioner.

The book will prove most useful to the physician who requires a one-volume reference on the problems of gynecology.

NOTICES

AMERICAN BOARD OF OPHTHALMOLOGY

Because of the war emergency, the American Board of Ophthalmology announces the following additional examinations: New York City, December 13 to 16, and Los Angeles, January 15 and 16.

At the last meeting, it was decided to cancel the 1943 written examination, to include in the oral examination all the subjects previously covered by the written examination and to dispense temporarily with the requirement of case reports. The oral examination will probably require two or three days and will cover the following subjects: external diseases (slip lamp); ophthalmoscopy; histology, pathology and bacteriology; ocular motility; refraction and retinoscopy; practical surgery; anatomy and embryology; perimetry; therapeutics and operations; optics and visual physiology; and relation of the eye to general diseases.

Formal application on the proper blanks for the December and January examinations must be filed with the secretary not later than November 1. Blanks may be obtained from the American Board of Ophthalmology, 6830 Waterman Avenue, St. Louis, Missouri.

YALE UNIVERSITY SCHOOL OF MEDICINE

A postgraduate course on industrial health and medicine in wartime will be given at Yale University School of Medicine on Wednesday afternoons from October 7 to December 23. Under the auspices of the Departments of Pharmacology, Preventive Medicine and Public Health, lectures and seminars will be presented by Drs. W. F. Von Oettingen, Leroy U. Gardner, R. A. Kehoe, Alice Hamilton, Louis Schwartz, Robert S. Goodhart, George R. Cowgill, C.-E. A. Winslow, M. I. Hall, Lydia Giberson, Louis Sachs, A. B. Landry and A. S. Gray; Lieutenant Colonels A. J. Lanza and D. B. Dill; and A. L. Coleman, Everett Martin, B. F. Postman, J. J. Bloomfield and E. P. Chester.

A registration fee of $10.00 will be charged, and those who attend the course regularly will be given a statement to that effect. Physicians who are interested may obtain detailed information from Dr. W. T. Salter, Yale University School of Medicine, New Haven, Connecticut.

LEWIS CASS LEDYARD, JR., FELLOWSHIP

The Lewis Cass Ledyard, Jr., Fellowship was established in 1939 by a gift from Mrs. Ruth E. Ledyard, wife of the late Lewis Cass Ledyard, Jr., a governor of the New York Hospital. The income, amounting to approximately $4000 annually, will be awarded to an investigator in the fields of medicine and surgery, or in any closely related field. This amount will be applied as follows: $3000 as a stipend and, approximately, $1000 for supplies or expenses of the research. In making the award, preference will be given to younger applicants who are graduates in medicine, and who have demonstrated fitness to carry on original research of high order. The recipient of this fellowship will be required to submit reports of his work under the fellowship, either at stated intervals or at the end of the academic year; and when the result of his work is published, he will be expected to give proper credit to the Lewis Cass Ledyard, Jr., Fellowship. The research work under this fellowship is to be carried on at the New York Hospital and Cornell University Medical College. The fellowship will be available on July 1 at the beginning of the academic year. Applications for the year 1943–1944 should be in the hands of the Committee by December 15. It is expected that the award will be made by March 15, 1943.

Application for this fellowship should be addressed to: Committee of the Lewis Cass Ledyard, Jr., Fellowship, The Society of the New York Hospital, 525 East Sixty-eighth Street, New York City.

SOCIETY MEETINGS AND CONFERENCES

Calendar of Boston District for the Week Beginning Sunday, August 30

Monday, August 31

12:15–1:15 p.m. Clinicopathological conference. Peter Bent Brigham Hospital amphitheater.

Tuesday, September 1

12:15–1:15 p.m. Clinicoroentgenologic conference. Peter Bent Brigham Hospital amphitheater.

Wednesday, September 2

*12:00 m. Clinicopathological conference. Children's Hospital.

*Open to the medical profession.

September 9–12. American Congress of Physical Therapy. Page x, issue of May 14.

September 29, 30 and October 1. Connecticut Clinical Congress. Yale Law School Building, New Haven, Connecticut.

September 30–October 10. Conference and Course in Legal Medicine. Mallory Institute of Pathology, Boston City Hospital. Page ix, issue of July 23.

October 7–December 23. Yale University School of Medicine. Notice above.

October 12–23. 1942 Graduate Fortnight. New York Academy of Medicine. Page xi, issue of May 21.

October 14–17. American Academy of Physical Medicine. Hotel Statler, Boston.

October 19–23. 1942 Clinical Congress of the American College of Surgeons. Page ix, issue of February 5.

October 21–24. Conference on Venereal-Disease-Control Needs in Wartime. Page ix, issue of August 20.

November 17–20. American College of Surgeons. Page ix, issue of August 20.

February 13. American Board of Obstetrics and Gynecology. Page ix, issue of July 2.

April 12–16. American College of Physicians. Page x, issue of July 16.

District Societies

BRISTOL SOUTH
December 3. Fall River.
May 6. New Bedford.

FRANKLIN
September 8.
November 10.
January 12.
March 9.
May 11. Annual meeting.
All meetings are held at 11:00 a.m. at the Franklin County Hospital, Greenfield.

MIDDLESEX NORTH
October 28.
January 27.
April 28.
July 28.

PLYMOUTH
October 15. Moore Hospital.
November 19. Plymouth County Hospital.
January 21. Brockton Hospital.
February 18. Jordan Hospital, Plymouth.
March 18. Goddard Hospital.
April 15. Bridgewater State Farm.
May 20. Lakeville.

WORCESTER
September 9. Belmont Hospital, Worcester.
October 14. Rutland State Sanatorium, Rutland.
November 11. Grafton State Hospital, North Grafton.
December 9. Worcester City Hospital, Worcester.
January 13. St. Vincent Hospital, Worcester.
February 10. Worcester State Hospital, Worcester.
March 10. Memorial Hospital, Worcester.
April 14. Hahnemann Hospital, Worcester.
May 12. Annual meeting.

WORCESTER NORTH
October 28.
January 27.
April 28.
July 28.

(Books Received on page ix)